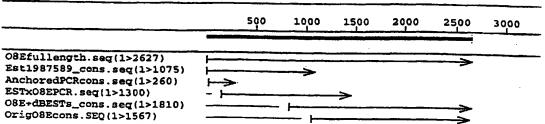
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(57) Abstract

Compositions and methods for the therapy and diagnosis of cancer, such as ovarian cancer, are disclosed. Compositions may comprise one or more ovarian carcinoma proteins, immunogenic portions thereof, polynucleotides that encode such portions or antibodies or immune system cells specific for such proteins. Such compositions may be used, for example, for the prevention and treatment of diseases such as ovarian cancer. Methods are further provided for identifying tumor antigens that are secreted from ovarian carcinomas and/or other tumors. Polypeptides and polynucleotides as provided herein may further be used for the diagnosis and monitoring of ovarian cancer.

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COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF OVARIAN CANCER

TECHNICAL FIELD

The present invention relates generally to ovarian cancer therapy. The invention is more specifically related to polypeptides comprising at least a portion of an ovarian carcinoma protein, and to polynucleotides encoding such polypeptides, as well as antibodies and immune system cells that specifically recognize such polypeptides. Such polypeptides, polynucleotides, antibodies and cells may be used in vaccines and pharmaceutical compositions for treatment of ovarian cancer.

BACKGROUND OF THE INVENTION 10

Ovarian cancer is a significant health problem for women in the United States and throughout the world. Although advances have been made in detection and therapy of this cancer, no vaccine or other universally successful method for prevention or treatment is currently available. Management of the disease currently relies on a combination of early diagnosis and aggressive treatment, which may include one or more of a variety of treatments such as surgery, radiotherapy, chemotherapy and hormone therapy. The course of treatment for a particular cancer is often selected based on a variety of prognostic parameters, including an analysis of specific tumor markers. However, the use of established markers often leads to a result that is difficult to interpret, and high mortality continues to be observed in many cancer patients.

Immunotherapies have the potential to substantially improve cancer treatment and survival. Such therapies may involve the generation or enhancement of an immune response to an ovarian carcinoma antigen. However, to date, relatively few ovarian carcinoma antigens are known and the generation of an immune response against such antigens has not been shown to be therapeutically beneficial.

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Accordingly, there is a need in the art for improved methods for identifying ovarian tumor antigens and for using such antigens in the therapy of ovarian cancer. The present invention fulfills these needs and further provides other related advantages.

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SUMMARY OF THE INVENTION

Briefly stated, this invention provides compositions and methods for the therapy of cancer, such as ovarian cancer. In one aspect, the present invention provides polypeptides comprising an immunogenic portion of an ovarian carcinoma protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with ovarian carcinoma protein-specific antisera is not substantially diminished. Within certain embodiments, the ovarian carcinoma protein comprises a sequence that is encoded by a polynucleotide sequence selected from the group consisting of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387, 391 and complements of such polynucleotides.

The present invention further provides polynucleotides that encode a polypeptide as described above or a portion thereof, expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions and vaccines. Pharmaceutical compositions may comprise a physiologically acceptable carrier or excipient in combination with one or more of: (i) a polypeptide comprising an immunogenic portion of an ovarian carcinoma protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with ovarian carcinoma proteinspecific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence encoded by a polynucleotide that comprises a sequence recited in any one of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387 or 391; (ii) a polynucleotide encoding such a polypeptide; (iii) an antibody that specifically binds to such a polypeptide; (iv) an antigen-presenting cell that expresses such a polypeptide and/or (y) a T cell that specifically reacts with such a polypeptide. Vaccines may comprise a non-specific immune response enhancer in combination with one or more of: (i) a polypeptide comprising an immunogenic portion of an ovarian carcinoma protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with ovarian carcinoma protein-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence encoded by a

polynucleotide that comprises a sequence recited in any one of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387 or 391; (ii) a polynucleotide encoding such a polypeptide; (iii) an anti-idiotypic antibody that is specifically bound by an antibody that specifically binds to such a polypeptide; (iv) an antigen-presenting cell that expresses such a polypeptide and/or (v) a T cell that specifically reacts with such a polypeptide.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

Within related aspects, pharmaceutical compositions comprising a fusion protein or polynucleotide encoding a fusion protein in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, comprising a fusion protein or polynucleotide encoding a fusion protein in combination with a non-specific immune response enhancer.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for stimulating and/or expanding T cells, comprising contacting T cells with (a) a polypeptide comprising an immunogenic portion of an ovarian carcinoma protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with ovarian carcinoma protein-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence encoded by a polynucleotide that comprises a sequence recited in any one of SEQ ID NOs:1-387 or 391; (b) a polynucleotide encoding such a polypeptide and/or (c) an antigen presenting cell that expresses such a polypeptide under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Such polypeptide, polynucleotide and/or antigen presenting cell(s) may be present within a pharmaceutical composition or vaccine, for use in stimulating and/or expanding T cells in a mammal.

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Within other aspects, the present invention provides methods for inhibiting the development of ovarian cancer in a patient, comprising administering to a patient T cells prepared as described above.

Within further aspects, the present invention provides methods for inhibiting the development of ovarian cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising an immunogenic portion of an ovarian carcinoma protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with ovarian carcinoma protein-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence encoded by a polynucleotide that comprises a sequence recited in any one of SEQ ID NOs: 1-387 or 391; (ii) a polynucleotide encoding such a polypeptide; or (iii) an antigen-presenting cell that expresses such a polypeptide; such that T cells proliferate; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of ovarian cancer in the patient. The proliferated cells may be cloned prior to administration to the patient.

The present invention also provides, within other aspects, methods for identifying secreted tumor antigens. Such methods comprise the steps of: (a) implanting tumor cells in an immunodeficient mammal; (b) obtaining serum from the immunodeficient mammal after a time sufficient to permit secretion of tumor antigens into the serum; (c) immunizing an immunocompetent mammal with the serum; (d) obtaining antiserum from the immunocompetent mammal; and (e) screening a tumor expression library with the antiserum, and therefrom identifying a secreted tumor antigen. A preferred method for identifying a secreted ovarian carcinoma antigen comprises the steps of: (a) implanting ovarian carcinoma cells in a SCID mouse; (b) obtaining serum from the SCID mouse after a time sufficient to permit secretion of ovarian carcinoma antigens into the serum; (c) immunizing an immunocompetent mouse with the serum; (d) obtaining antiserum from the immunocompetent mouse; and (e) screening an ovarian carcinoma expression library with the antiserum, and therefrom identifying a secreted ovarian carcinoma antigen.

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These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1A-1S (SEQ ID NOs:1-71) depict partial sequences of polynucleotides encoding representative secreted ovarian carcinoma antigens.

Figure 2A-2C depict full insert sequences for three of the clones of Figure 1. Figure 2A shows the sequence designated O7E (11731; SEQ ID NO:72), Figure 2B shows the sequence designated O9E (11785; SEQ ID NO:73) and Figure 2C shows the sequence designated O8E (13695; SEQ ID NO:74).

Figure 3 presents results of microarray expression analysis of the ovarian carcinoma sequence designated O8E.

Figure 4 presents a partial sequence of a polynucleotide (designated 3g; SEQ ID NO:75) encoding an ovarian carcinoma sequence that is a splice fusion between the human T-cell leukemia virus type I oncoprotein TAX and osteonectin.

Figure 5 presents the ovarian carcinoma polynucleotide designated 3f (SEQ ID NO:76).

Figure 6 presents the ovarian carcinoma polynucleotide designated 6b (SEQ ID NO:77).

Figures 7A and 7B present the ovarian carcinoma polynucleotides designated 8e (SEQ ID NO:78) and 8h (SEQ ID NO:79).

Figure 8 presents the ovarian carcinoma polynucleotide designated 12c (SEQ ID NO:80).

Figure 9 presents the ovarian carcinoma polynucleotide designated 12h (SEQ ID NO:81).

Figure 10 depicts results of microarray expression analysis of the ovarian carcinoma sequence designated 3f.

Figure 11 depicts results of microarray expression analysis of the ovarian carcinoma sequence designated 6b.

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Figure 12 depicts results of microarray expression analysis of the ovarian carcinoma sequence designated 8e.

Figure 13 depicts results of microarray expression analysis of the ovarian carcinoma sequence designated 12c.

Figure 14 depicts results of microarray expression analysis of the ovarian carcinoma sequence designated 12h.

Figures 15A-15EEE depict partial sequences of additional polynucleotides encoding representative secreted ovarian carcinoma antigens (SEQ ID NOs:82-310).

Figure 16 is a diagram illustrating the location of various partial O8E sequences within the full length sequence.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy of cancer, such as ovarian cancer. The compositions described herein may include immunogenic polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies that bind to a polypeptide, antigen presenting cells (APCs) and/or immune system cells (e.g., T cells).

Polypeptides of the present invention generally comprise at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof. Certain ovarian carcinoma proteins have been identified using an immunoassay technique, and are referred to herein as ovarian carcinoma antigens. An "ovarian carcinoma antigen" is a protein that is expressed by ovarian tumor cells (preferably human cells) at a level that is at least two fold higher than the level in normal ovarian cells. Certain ovarian carcinoma antigens react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera generated against serum from an immunodeficient animal implanted with a human ovarian tumor. Such ovarian carcinoma antigens are shed or secreted from an ovarian tumor into the sera of the immunodeficient animal. Accordingly, certain ovarian carcinoma antigens provided herein are secreted antigens. Certain nucleic acid sequences of the subject invention generally comprise a DNA or

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RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence.

The present invention further provides ovarian carcinoma sequences that are identified using techniques to evaluate altered expression within an ovarian tumor. Such sequences may be polynucleotide or protein sequences. Ovarian carcinoma sequences are generally expressed in an ovarian tumor at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in normal ovarian tissue, as determined using a representative assay provided herein. Certain partial ovarian carcinoma polynucleotide sequences are presented herein. Proteins encoded by genes comprising such polynucleotide sequences (or complements thereof) are also considered ovarian carcinoma proteins.

Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to at least a portion of an ovarian carcinoma polypeptide as described herein. T cells that may be employed within the compositions provided herein are generally T cells (e.g., CD4⁺ and/or CD8⁺) that are specific for such a polypeptide. Certain methods described herein further employ antigen-presenting cells (such as dendritic cells or macrophages) that express an ovarian carcinoma polypeptide as provided herein.

20 OVARIAN CARCINOMA POLYNUCLEOTIDES

Any polynucleotide that encodes an ovarian carcinoma protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides, and more preferably at least 45 consecutive nucleotides, that encode a portion of an ovarian carcinoma protein. More preferably, a polynucleotide encodes an immunogenic portion of an ovarian carcinoma protein, such as an ovarian carcinoma antigen. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a

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polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (i.e., an endogenous sequence that encodes an ovarian carcinoma protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native ovarian carcinoma protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native ovarian carcinoma protein or a portion thereof.

The percent identity for two polynucleotide or polypeptide sequences may be readily determined by comparing sequences using computer algorithms well known to those of ordinary skill in the art, such as Megalign, using default parameters. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, or 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. Optimal alignment of sequences for comparison may be conducted, for example, using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. Preferably, the percentage of sequence identity is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the window may comprise additions or deletions (i.e., gaps) of 20 % or less, usually 5 to 15 %, or 10 to 12%, relative to the reference sequence (which does not contain additions or deletions). The percent identity may be calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched

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positions by the total number of positions in the reference sequence (i.e., the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

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Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native ovarian carcinoma protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, an ovarian carcinoma polynucleotide may be identified, as described in more detail below, by screening a late passage ovarian tumor expression library with antisera generated against sera of immunocompetent mice after injection of such mice with sera from SCID mice implanted with late passage ovarian tumors. Ovarian carcinoma polynucleotides may also be identified using any of a variety of techniques designed to evaluate differential gene expression. Alternatively, polynucleotides may be amplified from cDNA prepared from ovarian tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific

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primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (e.g., an ovarian carcinoma cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with ³²P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., Molecular Cloning: A Laboratory Manual. Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining
a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be

sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (see Triglia et al., Nucl. Acids Res. 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Additional techniques include capture PCR (Lagerstrom et al., PCR Methods Applic. 1:111-19, 1991) and walking PCR (Parker et al., Nucl. Acids. Res. 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence.

Certain nucleic acid sequences of cDNA molecules encoding portions of ovarian carcinoma antigens are provided in Figures 1A-1S (SEQ ID NOS:1 to 71) and Figures 15A to 15EEE (SEQ ID NOS:82 to 310). The sequences provided in Figures 1A-1S appear to be novel. For sequences in Figures 15A-15EEE, database searches revealed matches having substantial identity. These polynucleotides were isolated by serological screening of an ovarian tumor cDNA expression library, using a technique designed to identify secreted tumor antigens. Briefly, a late passage ovarian tumor expression library was prepared from a SCID-derived human ovarian tumor (OV9334) in the vector λ-screen (Novagen). The sera used for screening were obtained by injecting immunocompetent mice with sera from SCID mice implanted with one late

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passage ovarian tumors. This technique permits the identification of cDNA molecules

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that encode immunogenic portions of secreted tumor antigens.

The polynucleotides recited herein, as well as full length polynucleotides

omprising such sequences, other portions of such full length polynucleotides, and sequences complementary to all or a portion of such full length molecules, are specifically encompassed by the present invention. It will be apparent to those of ordinary skill in the art that this technique can also be applied to the identification of antigens that are secreted from other types of tumors.

Other nucleic acid sequences of cDNA molecules encoding portions of ovarian carcinoma proteins are provided in Figures 4-9 (SEQ ID NOs:75-81), as well as SEQ ID NOs:313-384. These sequences were identified by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least five fold greater in an ovarian tumor than in normal ovarian tissue, as determined using a representative assay provided herein). Such screens were performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA 94*:2150-2155, 1997). SEQ ID NOs:311 and 391 provide full length sequences incorporating certain of these nucleic acid sequences.

Any of a variety of well known techniques may be used to evaluate tumor-associated expression of a cDNA. For example, hybridization techniques using labeled polynucleotide probes may be employed. Alternatively, or in addition, amplification techniques such as real-time PCR may be used (see Gibson et al., Genome Research 6:995-1001, 1996; Heid et al., Genome Research 6:986-994, 1996). Real-time PCR is a technique that evaluates the level of PCR product accumulation during amplification. This technique permits quantitative evaluation of mRNA levels in multiple samples. Briefly, mRNA is extracted from tumor and normal tissue and cDNA is prepared using standard techniques. Real-time PCR may be performed, for example, using a Perkin Elmer/Applied Biosystems (Foster City, CA) 7700 Prism instrument. Matching primers and fluorescent probes may be designed for genes of interest using, for example, the primer express program provided by Perkin Elmer/Applied Biosystems (Foster City, CA). Optimal concentrations of primers and probes may be initially

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determined by those of ordinary skill in the art, and control (e.g., β-actin) primers and probes may be obtained commercially from, for example, Perkin Elmer/Applied Biosystems (Foster City, CA). To quantitate the amount of specific RNA in a sample, a standard curve is generated alongside using a plasmid containing the gene of interest. Standard curves may be generated using the Ct values determined in the real-time PCR, which are related to the initial cDNA concentration used in the assay. Standard dilutions ranging from 10-10⁶ copies of the gene of interest are generally sufficient. In addition, a standard curve is generated for the control sequence. This permits standardization of initial RNA content of a tissue sample to the amount of control for comparison purposes.

Polynucleotide variants may generally be prepared by any method known in the artificial synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see Adelman et al., DNA 2:183, 1983). Alternatively, RNA molecules may be generated by in vitro or in vivo transcription of DNA sequences encoding an ovarian carcinoma antigen, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated in vivo.

A portion of a sequence complementary to a coding sequence (i.e., an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells or tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of an ovarian carcinoma protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (see Gee et al., In Huber and Carr, Molecular and Immunologic Approaches, Futura Publishing Co. (Mt. Kisco, NY; 1994). Alternatively, an antisense molecule

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may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

Any polynucleotide may be further modified to increase stability in vivo. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may

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also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

10 OVARIAN CARCINOMA POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof, as described herein. As noted above, certain ovarian carcinoma proteins are ovarian carcinoma antigens that are expressed by ovarian tumor cells and react detectably within an immunoassay (such as an ELISA) with antisera generated against serum from an immunodeficient animal implanted with an ovarian tumor. Other ovarian carcinoma proteins are encoded by ovarian carcinoma polynucleotides recited herein. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of an antigen that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of an ovarian carcinoma protein or a variant thereof. Preferred immunogenic portions are encoded by cDNA molecules isolated as described herein. Further immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with ovarian carcinoma protein-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "ovarian carcinoma

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protein-specific" if they specifically bind to an ovarian carcinoma protein (*i.e.*, they react with the ovarian carcinoma protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera, antibodies and T cells may be prepared as described herein, and using well known techniques. An immunogenic portion of a native ovarian carcinoma protein is a portion that reacts with such antisera, antibodies and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length protein. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

As noted above, a composition may comprise a variant of a native ovarian carcinoma protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native ovarian carcinoma protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with ovarian carcinoma protein-specific antisera may be enhanced or unchanged, relative to the native ovarian carcinoma protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native ovarian carcinoma protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with ovarian carcinoma protein-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

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Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity to the native polypeptide. Preferably, a variant contains conservative substitutions. "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host

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cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, J. Am. Chem. Soc. 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Applied BioSystems, Inc. (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises one polypeptide as described herein and a known tumor antigen, such as an ovarian carcinoma protein or a variant of such a protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a

recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., Gene 40:39-46, 1985; Murphy et al., Proc. Natl. Acad. Sci. USA 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

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Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. New Engl. J. Med., 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium Haemophilus influenza B (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (e.g., the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in E. coli (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen present cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemaglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the LytA gene; *Gene 43*:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology 10*:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

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In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

10 BINDING AGENTS

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The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to an ovarian carcinoma protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to an ovarian carcinoma protein if it reacts at a detectable level (within, for example, an ELISA) with an ovarian carcinoma protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a "complex" is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10³ L/mol. The binding constant maybe determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as ovarian cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a ovarian carcinoma antigen will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological

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samples (e.g., blood, sera, leukophoresis, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the

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desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ⁹⁰Y, ¹²³I, ¹²⁵I, ¹³¹I, ¹⁸⁶Re, ¹⁸⁸Re, ²¹¹At, and ²¹²Bi. Preferred drugs include

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methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diptheria toxin, cholera toxin, gelonin, Pseudomonas exotoxin, Shigella toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (e.g., covalently bonded) to a suitable monoclonal antibody either directly or indirectly (e.g., via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (e.g., a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, e.g., U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (e.g., U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (e.g., U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of

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derivatized amino acid side chains (e.g., U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (e.g., U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (e.g., U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (e.g., U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (e.g., U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (e.g., U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

Also provided herein are anti-idiotypic antibodies that mimic an immunogenic portion of an ovarian carcinoma protein. Such antibodies may be raised against an antibody, or antigen-binding fragment thereof, that specifically binds to an

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immunogenic portion of an ovarian carcinoma protein, using well known techniques. Anti-idiotypic antibodies that mimic an immunogenic portion of an ovarian carcinoma protein are those antibodies that bind to an antibody, or antigen-binding fragment thereof, that specifically binds to an immunogenic portion of an ovarian carcinoma protein, as described herein.

T CELLS

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Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for an ovarian carcinoma protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be present within (or isolated from) bone marrow, peripheral blood or a fraction of bone marrow or peripheral blood of a mammal, such as a patient, using a commercially available cell separation system, such as the CEPRATE™ system, available from CellPro Inc., Bothell WA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human animals, cell lines or cultures.

T cells may be stimulated with an ovarian carcinoma polypeptide, polynucleotide encoding an ovarian carcinoma polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, an ovarian carcinoma polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for an ovarian carcinoma polypeptide if the T cells kill target cells coated with an ovarian carcinoma polypeptide or expressing a gene encoding such a polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be

accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with an ovarian carcinoma polypeptide (200 ng/ml - 100 μ g/ml, preferably 100 ng/ml - 25 μ g/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells and/or contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-y) is indicative of T cell activation (see Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998). T cells that have been activated in response to an ovarian carcinoma polypeptide, polynucleotide or ovarian carcinoma polypeptide-expressing APC may be CD4+ and/or CD8+. Ovarian carcinoma polypeptide-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from a patient or a related or unrelated donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to an ovarian carcinoma polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to an ovarian carcinoma polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize an ovarian carcinoma polypeptide. Alternatively, one or more T cells that proliferate in the presence of an ovarian carcinoma polypeptide can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution. Following expansion, the cells may be administered back to the patient as described, for example, by Chang et al., *Crit. Rev. Oncol. Hematol. 22*:213, 1996.

PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, binding agents and/or immune system cells as described herein may be incorporated into

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pharmaceutical compositions or vaccines. Pharmaceutical compositions comprise one or more such compounds or cells and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds or cells and a non-specific immune response enhancer. A non-specific immune response enhancer may be any substance that enhances an immune response to an exogenous antigen. Examples of non-specific immune response enhancers include adjuvants, biodegradable microspheres (e.g., polylactic galactide) and liposomes (into which the compound is incorporated; see e.g., Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated in situ. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as Bacillus-Calmette-Guerrin) that expresses an immunogenic portion of the polypeptide on its cell surface. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., PNAS 86:317-321, 1989; Flexner et al., Ann. N.Y. Acad. Sci. 569:86-103, 1989; Flexner et al., Vaccine 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, Biotechniques 6:616-627, 1988; Rosenfeld et al., Science 252:431-434, 1991; Kolls et al., PNAS 91:215-219, 1994; Kass-Eisler et al.,

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PNAS 90:11498-11502, 1993; Guzman et al., Circulation 88:2838-2848, 1993; and Guzman et al., Cir. Res. 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., Science 259:1745-1749, 1993 and reviewed by Cohen, Science 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of non-specific immune response enhancers may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune

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responses, such as lipid A, Bortadella pertussis or Mycobacterium tuberculosis derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI), Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ), alum, biodegradable microspheres, monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN-γ, IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6, IL-10 and TNF-β) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). Also preferred is AS-2 (SmithKline Beecham). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO

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96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule or sponge that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent

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APCs (Banchereau and Steinman, *Nature 392*:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med. 50*:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*) and based on the lack of differentiation markers of B cells (CD19 and CD20), T cells (CD3), monocytes (CD14) and natural killer cells (CD56), as determined using standard assays. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see Zitvogel et al.*, *Nature Med. 4:*594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNFα to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNFα, CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fcy receptor, mannose receptor and DEC-205 marker. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell

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activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80 and CD86).

APCs may generally be transfected with a polynucleotide encoding a ovarian carcinoma antigen (or portion or other variant thereof) such that the antigen, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place ex vivo, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs in vivo. In vivo and ex vivo transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., Immunology and cell Biology 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (e.g., a carrier Alternatively, a dendritic cell may be pulsed with a non-conjugated molecule). immunological partner, separately or in the presence of the polypeptide.

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CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as ovarian cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. Within certain preferred embodiments, a patient is afflicted with ovarian cancer. Such cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or

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following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immuno response-modifying agents (such as tumor vaccines, bacterial adjuvants and/or cytokines).

Within embodiments, other immunotherapy may be immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T lymphocytes (such as CD8+ cytotoxic T lymphocytes and CD4+ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example,

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antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow in vivo and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al., Immunological Reviews 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into stem cells taken from a patient and clonally propagated *in vitro* for autologous transplant back into the same patient.

Routes and frequency of administration, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (e.g., intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (e.g., by aspiration), orally or in the bed of a resected tumor. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (i.e., untreated) level.. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells in vitro. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (e.g., more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 100 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

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In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (e.g., more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to an ovarian carcinoma antigen generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

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SCREENS FOR IDENTIFYING SECRETED OVARIAN CARCINOMA ANTIGENS

The present invention provides methods for identifying secreted tumor antigens. Within such methods, tumors are implanted into immunodeficient animals such as SCID mice and maintained for a time sufficient to permit secretion of tumor antigens into serum. In general, tumors may be implanted subcutaneously or within the gonadal fat pad of an immunodeficient animal and maintained for 1-9 months, preferably 1-4 months. Implantation may generally be performed as described in WO 97/18300. The serum containing secreted antigens is then used to prepare antisera in immunocompetent mice, using standard techniques and as described herein. Briefly, 50-100 µL of sera (pooled from three sets of immunodeficient mice, each set bearing a different SCID-derived human ovarian tumor) may be mixed 1:1 (vol:vol) with an appropriate adjuvant, such as RIBI-MPL or MPL + TDM (Sigma Chemical Co., St. Louis, MO) and injected intraperitoneally into syngeneic immunocompetent animals at monthly intervals for a total of 5 months. Antisera from animals immunized in such a manner may be obtained by drawing blood after the third, fourth and fifth immunizations. The resulting antiserum is generally pre-cleared of E. coli and phage antigens and used (generally following dilution, such as 1:200) in a serological expression screen.

The library is typically an expression library containing cDNAs from one or more tumors of the type that was implanted into SCID mice. This expression library may be prepared in any suitable vector, such as λ -screen (Novagen). cDNAs that

encode a polypeptide that reacts with the antiserum may be identified using standard techniques, and sequenced. Such cDNA molecules may be further characterized to evaluate expression in tumor and normal tissue, and to evaluate antigen secretion in patients.

The methods provided herein have advantages over other methods for tumor antigen discovery. In particular, all antigens identified by such methods should be secreted or released through necrosis of the tumor cells. Such antigens may be present on the surface of tumor cells for an amount of time sufficient to permit targeting and killing by the immune system, following vaccination.

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METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more ovarian carcinoma proteins and/or polynucleotides encoding such proteins in a biological sample (such as blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as ovarian cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of protein that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, an ovarian carcinoma-associated sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

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In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the WO 00/36107 PCT/US99/30270

remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length ovarian carcinoma proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about

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 $10\,\mu g$, and preferably about $100\,n g$ to about $1\,\mu g$, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20^{TM} (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with ovarian cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve

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equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20TM. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as ovarian cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot

of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1µg, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

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may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with an ovarian carcinoma protein in a biological sample. Within certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with an ovarian carcinoma protein, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated in vitro for 2-9 days (typically 4 days) at 37°C with an ovarian carcinoma protein (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of ovarian carcinoma protein to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding an ovarian carcinoma protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of an ovarian carcinoma protein cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the ovarian carcinoma protein. The amplified cDNA is then separated and detected using techniques well

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known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding an ovarian carcinoma protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding an ovarian carcinoma protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably. oligonucleotide primers and/or probes hybridize to a polynucleotide encoding a polypeptide described herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence provided herein. Techniques for both PCR based assays and hybridization assays are well known in the art (see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample such as a biopsy tissue and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, ovarian carcinoma proteins and polynucleotides encoding such proteins may be used as markers for monitoring the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide detected by the binding agent increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple ovarian carcinoma protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

DIAGNOSTIC KITS

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The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to an ovarian carcinoma protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively,

contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding an ovarian carcinoma protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding an ovarian carcinoma protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding an ovarian carcinoma protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

Example 1

Identification of Representative Ovarian Carcinoma Protein cDNAs

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This Example illustrates the identification of cDNA molecules encoding ovarian carcinoma proteins.

Anti-SCID mouse sera (generated against sera from SCID mice carrying late passage ovarian carcinoma) was pre-cleared of E. coli and phage antigens and used at a 1:200 dilution in a serological expression screen. The library screened was made from a SCID-derived human ovarian tumor (OV9334) using a directional RH oligo(dT) priming cDNA library construction kit and the λScreen vector (Novagen). A bacteriophage lambda screen was employed. Approximately 400,000 pfu of the amplified OV9334 library were screened.

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196 positive clones were isolated. Certain sequences that appear to be novel are provided in Figures 1A-1S and SEQ ID NOs:1 to 71. Three complete insert sequences are shown in Figures 2A-2C (SEQ ID NOs:72 to 74). Other clones having known sequences are presented in Figures 15A-15EEE (SEQ ID NOs:82 to 310). Database searches identified the following sequences that were substantially identical to the sequences presented in Figures 15A-15EEE.

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These clones were further characterized using microarray technology to determine mRNA expression levels in a variety of tumor and normal tissues. Such analyses were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions. PCR amplification products were arrayed on slides, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes and the slides were scanned to measure fluorescence intensity. Data was analyzed using Synteni's provided GEMtools software. The results for one clone (13695, also referred to as O8E) are shown in Figure 3.

Example 2

Identification of Ovarian Carcinoma cDNAs using Microarray Technology

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This Example illustrates the identification of ovarian carcinoma polynucleotides by PCR subtraction and microarray analysis. Microarrays of cDNAs were analyzed for ovarian tumor-specific expression using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA 94*:2150-2155, 1997).

A PCR subtraction was performed using a tester comprising cDNA of four ovarian tumors (three of which were metastatic tumors) and a driver of cDNA form five normal tissues (adrenal gland, lung, pancreas, spleen and brain). cDNA fragments recovered from this subtraction were subjected to DNA microarray analysis where the fragments were PCR amplified, adhered to chips and hybridized with fluorescently labeled probes derived from mRNAs of human ovarian tumors and a variety of normal human tissues. In this analysis, the slides were scanned and the fluorescence intensity was measured, and the data were analyzed using Synteni's GEMtools software. In general, sequences showing at least a 5-fold increase in expression in tumor cells (relative to normal cells) were considered ovarian tumor antigens. The fluorescent results were analyzed and clones that displayed increased expression in ovarian tumors were further characterized by DNA sequencing and database searches to determine the novelty of the sequences.

Using such assays, an ovarian tumor antigen was identified that is a splice fusion between the human T-cell leukemia virus type I oncoprotein TAX (see Jin et al., Cell 93:81-91, 1998) and an extracellular matrix protein called osteonectin. A splice junction sequence exists at the fusion point. The sequence of this clone is presented in Figure 4 and SEQ ID NO:75. Osteonectin, unspliced and unaltered, was also identified from such assays independently.

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Further clones identified by this method are referred to herein as 3f, 6b, 8e, 8h, 12c and 12h. Sequences of these clones are shown in Figures 5 to 9 and SEQ ID NOs:76 to 81. Microarray analyses were performed as described above, and are presented in Figures 10 to 14. A full length sequence encompassing clones 3f, 6b, 8e and 12h was obtained by screening an ovarian tumor (SCID-derived) cDNA library. This 2996 base pair sequence (designated O772P) is presented in SEQ ID NO:311, and the encoded 914 amino acid protein sequence is shown in SEQ ID NO:312. PSORT analysis indicates a Type 1a transmembrane protein localized to the plasma membrane.

In addition to certain of the sequences described above, this screen identified the following sequences:

Sequence	Comments
OV4vG11 (SEQ ID NO:313)	human clone 1119D9 on chromosome 20p12
OV4vB11 (SEQ ID NO:314)	human UWGC:y14c094 from chromosome 6p21
OV4vD9 (SEQ ID NO:315)	human clone 1049G16 chromosome 20q12-13.2
OV4vD5 (SEQ ID NO:316)	human KIAA0014 gene
OV4vC2 (SEQ ID NO:317)	human KIAA0084 gene
OV4vF3 (SEQ ID NO:318)	human chromosome 19 cosmid R31167
OV4VC1 (SEQ ID NO:319)	novel
OV4vH3 (SEQ ID NO:320)	novel
OV4vD2 (SEQ ID NO:321)	novel
O815P (SEQ ID NO:322)	novel
OV4vC12 (SEQ ID NO:323)	novel
OV4vA4 (SEQ ID NO:324)	novel
OV4vA3 (SEQ ID NO:325)	novel
OV4v2A5 (SEQ ID NO:326)	novel
O819P (SEQ ID NO:327)	novel
O818P (SEQ ID NO:328)	novel
O817P (SEQ ID NO:329)	novel
O816P (SEQ ID NO:330)	novel
Ov4vC5 (SEQ ID NO:331)	novel

Sequence	Comments
21721 (SEQ ID NO:332)	human lumican
21719 (SEQ ID NO:333)	human retinoic acid-binding protein II
21717 (SEQ ID NO:334)	human26S proteasome ATPase subunit
21654 (SEQ ID NO:335)	human copine I
21627 (SEQ ID NO:336)	human neuron specific gamma-2 enolase
21623 (SEQ ID NO:337)	human geranylgeranyl transferase II
21621 (SEQ ID NO:338)	human cyclin-dependent protein kinase
21616 (SEQ ID NO:339)	human prepro-megakaryocyte potentiating factor
21612 (SEQ ID NO:340)	human UPH1
21558 (SEQ ID NO:341)	human RalGDS-like 2 (RGL2)
21555 (SEQ ID NO:342)	human autoantigen P542
21548 (SEQ ID NO:343)	human actin-related protein (ARP2)
21462 (SEQ ID NO:344)	human huntingtin interacting protein
21441 (SEQ ID NO:345)	human 90K product (tumor associated antigen)
21439 (SEQ ID NO:346)	human guanine nucleotide regulator protein (tim1)
21438 (SEQ ID NO:347)	human Ku autoimmune (p70/p80) antigen
21237 (SEQ ID NO:348)	human S-laminin
21436 (SEQ ID NO:349)	human ribophorin I
21435 (SEQ ID NO:350)	human cytoplasmic chaperonin hTRiC5
21425 (SEQ ID NO:351)	humanEMX2
21423 (SEQ ID NO:352)	human p87/p89 gene
21419 (SEQ ID NO:353)	human HPBRII-7
21252 (SEQ ID NO:354)	human T1-227H
21251 (SEQ ID NO:355)	human cullin I
21247 (SEQ ID NO:356)	kunitz type protease inhibitor (KOP)
21244-1 (SEQ ID NO:357)	human protein tyrosine phosphatase receptor F (PTPRF)
21718 (SEQ ID NO:358)	human LTR repeat
OV2-90 (SEQ ID NO:359)	novel

Sequence	Comments	
Human zinc finger (SEQ ID NO:	360)	
Human polyA binding protein (SEQ ID NO:361)		
Human pleitrophin (SEQ ID NO:362)		
Human PAC clone 278C19 (SEQ ID NO:363)		
Human LLRep3 (SEQ ID NO:364)		
Human Kunitz type protease inhib (SEQ ID NO:365)		
Human KIAA0106 gene (SEQ ID NO:366)		
Human keratin (SEQ ID NO:367)		
Human HIV-1TAR (SEQ ID NO:	368)	
Human glia derived nexin (SEQ I	D NO:369)	
Human fibronectin (SEQ ID NO::	370)	
Human ECMproBM40 (SEQ ID NO:371)		
Human collagen (SEQ ID NO:372	2)	
Human alpha enolase (SEQ ID No	0:373)	
Human aldolase (SEQ ID NO:374	1)	
Human transf growth factor BIG I	H3 (SEQ ID NO:375)	
Human SPARC osteonectin (SEQ	ID NO:376)	
Human SLP1 leucocyte protease (SEQ ID NO:377)		
Human mitochondrial ATP synth (SEQ ID NO:378)		
Human DNA seq clone 461P17 (SEQ ID NO:379)		
Human dbpB pro Y box (SEQ ID NO:380)		
Human 40 kDa keratin (SEQ ID N	IO:381)	
Human arginosuccinate synth (SE		
Human acidic ribosomal phosphoprotein (SEQ ID NO:383)		
Human colon carcinoma laminin b	pinding pro (SEQ ID NO:384)	

This screen further identified multiple forms of the clone O772P, referred to herein as 21013, 21003 and 21008. PSORT analysis indicates that 21003 (SEQ ID NO:386; translated as SEQ ID NO:389) and 21008 (SEQ ID NO:387; translated as SEQ ID NO:390) represent Type 1a transmembrane protein forms of

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O772P. 21013 (SEQ ID NO:385; translated as SEQ ID NO:388) appears to be a truncated form of the protein and is predicted by PSORT analysis to be a secreted protein.

Additional sequence analysis resulted in a full length clone for O8E (2627 bp, which agrees with the message size observed by Northern analysis; SEQ ID NO:391). This nucleotide sequence was obtained as follows: the original O8E sequence (OrigO8Econs) was found to overlap by 33 nucleotides with a sequence from an EST clone (IMAGE#1987589). This clone provided 1042 additional nucleotides upstream of the original O8E sequence. The link between the EST and O8E was confirmed by sequencing multiple PCR fragments generated from an ovary primary tumor library using primers to the unique EST and the O8E sequence (ESTxO8EPCR). Full length status was further indicated when anchored PCR from the ovary tumor library gave several clones (AnchoredPCR cons) that all terminated upstream of the putative start methionine, but failed to yield any additional sequence information. Figure 16 presents a diagram that illustrates the location of each partial sequence within the full length O8E sequence.

Two protein sequences may be translated from the full length O8E. For "a" (SEQ ID NO:393) begins with a putative start methionine. A second form—"b" (SEQ ID NO:392) includes 27 additional upstream residues to the 5' end of the nucleotide sequence.

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

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SUMMARY OF SEQUENCE LISTING

SEQ ID NOs:1-71 are ovarian carcinoma antigen polynucleotides shown in Figures 1A-1S.

SEQ ID NOs:72-74 are ovarian carcinoma antigen polynucleotides shown in Figures 2A-2C.

SEQ ID NO:75 is the ovarian carcinoma polynucleotide 3g (Figure 4).

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SEQ ID NO:76 is the ovarian carcinoma polynucleotide 3f (Figure 5).

SEQ ID NO:77 is the ovarian carcinoma polynucleotide 6b (Figure 6).

SEQ ID NO:78 is the ovarian carcinoma polynucleotide 8e (Figure 7A).

SEQ ID NO:79 is the ovarian carcinoma polynucleotide 8h (Figure 7B).

SEQ ID NO:80 is the ovarian carcinoma polynucleotide 12e (Figure 8).

SEQ ID NO:81 is the ovarian carcinoma polynucleotide 12h (Figure 9).

SEQ ID NOs:82-310 are ovarian carcinoma antigen polynucleotides shown in Figures 15A-15EEE.

SEQ ID NO:311 is a full length sequence of ovarian carcinoma polynucleotide O772P.

SEQ ID NO:312 is the O772P amino acid sequence.

SEQ ID NOs:313-384 are ovarian carcinoma antigen polynucleotides.

SEQ ID NOs:385-390 present sequences of O772P forms.

SEQ ID NO:391 is a full length sequence of ovarian carcinoma polynucleotide O8E.

SEQ ID NOs:392-393 are protein sequences encoded by O8E.

CLAIMS

- 1. An isolated polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigenspecific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (a) polynucleotides recited in any one of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387 or 391; and
 - (b) complements of the foregoing polynucleotides.
- 2. A polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (a) polynucleotides recited in any one of 1-81, 313-331, 359, 366, 379, 385-387 or 391; and
 - (b) complements of such polynucleotides.
- 3. An isolated polynucleotide encoding at least 5 amino acid residues of a polypeptide according to claim polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigenspecific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (a) polynucleotides recited in any one of SEQ ID NOs:1-81, 319-331, 359, 385-387 or 391; and
 - (b) complements of the foregoing polynucleotides

- 4. A polynucleotide according to claim 3, wherein the polynucleotide encodes an immunogenic portion of the polypeptide.
- 5. A polynucleotide according to claim 3, wherein the polynucleotide comprises a sequence recited in any one of SEQ ID NOs:1-81, 319-331, 359, 385-387, 391 or a complement of any of the foregoing sequences.
- 6. An isolated polynucleotide complementary to a polynucleotide according to claim 3.
- 7. An expression vector comprising a polynucleotide according to claim 3 or claim 6.
- 8. A host cell transformed or transfected with an expression vector according to claim 7.
- 9. A pharmaceutical composition comprising a polypeptide according to claim 1, in combination with a physiologically acceptable carrier.
- 10. A pharmaceutical composition according to claim 9, wherein the polypeptide comprises an amino acid sequence encoded by a polynucleotide that comprises a sequence recited in any one of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387 or 391.
- 11. A vaccine comprising a polypeptide according to claim 1, in combination with a non-specific immune response enhancer.
- 12. A vaccine according to claim 11, wherein the polypeptide comprises an amino acid sequence encoded by a polynucleotide that comprises a sequence recited in any one of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387 or 391.
 - 13. A pharmaceutical composition comprising:

- (a) a polynucleotide encoding an ovarian carcinoma polypeptide, wherein the polypeptide comprises at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-81, 319-331, 359, 385-387 or 391; and
 - (ii) complements of the foregoing polynucleotides; and
 - (b) a physiologically acceptable carrier.
- 14. A pharmaceutical composition according to claim 13, wherein the polynucleotide comprises a sequence recited in any one of SEQ ID NOs:1-81, 319-331, 359, 385-387, 391 or a complement of any of the foregoing sequences.
 - 15. A vaccine comprising:
- (a) a polynucleotide encoding an ovarian carcinoma polypeptide, wherein the polypeptide comprises at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387 or 391; and
 - (ii) complements of the foregoing polynucleotides; and
- 16. A vaccine according to claim 15, wherein the polynucleotide comprises a sequence recited in any one of SEQ ID NOs:1-81. 319-331, 359, 385-387 or 391.
 - 17. A pharmaceutical composition comprising:

- (a) an antibody that specifically binds to an ovarian carcinoma protein, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-81, 313-331, 359, 366, 379, 385-387 or 391; and
 - (ii) complements of such polynucleotides; and
 - (b) a physiologically acceptable carrier.
- 18. A method for inhibiting the development of ovarian cancer in a patient, comprising administering to a patient an effective amount of an agent selected from the group consisting of:
- (a) an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
 - (ii) complements of such polynucleotides;
 - (b) a polynucleotide encoding a polypeptide as recited in (a); and
- (c) an antibody that specifically binds to an ovarian carcinoma protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
 - (ii) complements of such polynucleotides; and thereby inhibiting the development of ovarian cancer in the patient.

- 19. A method according to claim 18, wherein the agent is present within a pharmaceutical composition according to any one of claims 9, 13 or 17.
- 20. A method according to claim 18, wherein the agent is present within a vaccine according to any one of claims 11, 15 or 18.
- 21. A fusion protein comprising at least one polypeptide according to claim 1.
 - 22. A polynucleotide encoding a fusion protein according to claim 21.
- 23. A pharmaceutical composition comprising a fusion protein according to claim 21 in combination with a physiologically acceptable carrier.
- 24. A vaccine comprising a fusion protein according to claim 21 in combination with a non-specific immune response enhancer.
- 25. A pharmaceutical composition comprising a polynucleotide according to claim 22 in combination with a physiologically acceptable carrier.
- 26. A vaccine comprising a polynucleotide according to claim 22 in combination with a non-specific immune response enhancer.
- 27. A method for inhibiting the development of ovarian cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 23 or claim 25.
- 28. A method for inhibiting the development of ovarian cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 23 or claim 26.

- 29. A pharmaceutical composition, comprising:
- (a) an antigen presenting cell that expresses an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
 - (ii) complements of such polynucleotides; and
 - (b) a pharmaceutically acceptable carrier or excipient.
 - 30. A vaccine, comprising:
- (a) an antigen presenting cell that expresses an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
 - (ii) complements of such polynucleotides; and
 - (b) a non-specific immune response enhancer.
 - 31. A vaccine comprising:
- (a) an anti-idiotypic antibody or antigen-binding fragment thereof that is specifically bound by an antibody that specifically binds to an ovarian carcinoma protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and

- (ii) complements of such polynucleotides; and
- (b) non-specific immune response enhancer.
- 32. A vaccine according to claim 30 or claim 31, wherein the immune response enhancer is an adjuvant.
 - 33. A pharmaceutical composition, comprising:
- (a) a T cell that specifically reacts with an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
 - (ii) complements of such polynucleotides; and
 - (b) a physiologically acceptable carrier.
 - 34. A vaccine, comprising:
- (a) a T cell that specifically reacts with an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
 - (ii) complements of such polynucleotides; and
 - (b) a non-specific immune response enhancer.

- 35. A method for inhibiting the development of ovarian cancer in a patient, comprising administering to the patient an effective amount of a pharmaceutical composition according to claim 29 or claim 33.
- 36. A method for inhibiting the development of ovarian cancer in a patient, comprising administering to the patient an effective amount of a vaccine according to any one of claims 30, 31 or 34.
- 37. A method for stimulating and/or expanding T cells, comprising contacting T cells with:
- (a) an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
 - (ii) complements of such polynucleotides;
 - (b) a polynucleotide encoding such a polypeptide; and/or
- (c) an antigen presenting cell that expresses such a polypeptide under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.
- 38. A method according to claim 37, wherein the T cells are cloned prior to expansion.
- 39. A method for stimulating and/or expanding T cells in a mammal, comprising administering to a mammal a pharmaceutical composition comprising:
 - (a) one or more of:
- (i) an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one

or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

polynucleotides recited in any one of SEQ ID NOs:1-387 or

391; and

complements of such polynucleotides;

(ii) a polynucleotide encoding an ovarian carcinoma polypeptide;

or

- (iii) an antigen-presenting cell that expresses an ovarian carcinoma polypeptide; and
 - (b) a physiologically acceptable carrier or excipient; and thereby stimulating and/or expanding T cells in a mammal.
- 40. A method for stimulating and/or expanding T cells in a mammal, comprising administering to a mammal a vaccine comprising:
 - (a) one or more of:
- (i) an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

polynucleotides recited in any one of SEQ ID NOs:1-387 or

391; and

or

complements of such polynucleotides;

- (ii) a polynucleotide encoding an ovarian carcinoma polypeptide;
- (iii) an antigen-presenting cell that expresses an ovarian carcinoma polypeptide; and

- (b) a non-specific immune response enhancer; and thereby stimulating and/or expanding T cells in a mammal.
- 41. A method for inhibiting the development of ovarian cancer in a patient, comprising administering to a patient T cells prepared according to the method of claim 39 or claim 40.
- 42. A method for inhibiting the development of ovarian cancer in a patient, comprising the steps of:
 - (a) incubating CD4⁺ T cells isolated from a patient with one or more of:
- (i) an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and

complements of such polynucleotides;

- (ii) a polynucleotide encoding an ovarian carcinoma polypeptide;
- (iii) an antigen-presenting cell that expresses an ovarian carcinoma polypeptide;

such that T cells proliferate; and

- (b) administering to the patient an effective amount of the proliferated T cells, and therefrom inhibiting the development of ovarian cancer in the patient.
- 43. A method for inhibiting the development of ovarian cancer in a patient, comprising the steps of:
 - (a) incubating CD4⁺ T cells isolated from a patient with one or more of:

or

(i) an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

polynucleotides recited in any one of SEQ ID NOs:1-387 or

391; and

complements of such polynucleotides;

(ii) a polynucleotide encoding an ovarian carcinoma polypeptide;

or

(iii) an antigen-presenting cell that expresses an ovarian carcinoma polypeptide;

such that T cells proliferate;

- (b) cloning one or more proliferated cells; and
- (c) administering to the patient an effective amount of the cloned T cells.
- 44. A method for inhibiting the development of ovarian cancer in a patient, comprising the steps of:
 - (a) incubating CD8⁺ T cells isolated from a patient with one or more of:
- (i) an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

polynucleotides recited in any one of SEQ ID NOs:1-387 or

391; and

complements of such polynucleotides;

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- (ii) a polynucleotide encoding an ovarian carcinoma polypeptide;
- an antigen-presenting cell that expresses an ovarian carcinoma (iii) polypeptide;

such that T cells proliferate; and

- administering to the patient an effective amount of the proliferated T cells, and therefrom inhibiting the development of ovarian cancer in the patient.
- 45. A method for inhibiting the development of ovarian cancer in a patient, comprising the steps of:
 - incubating CD8+ T cells isolated from a patient with one or more of: (a)
- an ovarian carcinoma polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and

complements of such polynucleotides;

- (ii) a polynucleotide encoding an ovarian carcinoma polypeptide;
- (iii) an antigen-presenting cell that expresses an ovarian carcinoma polypeptide;

such that the T cells proliferate;

- (b) cloning one or more proliferated cells; and
- (c) administering to the patient an effective amount of the cloned T cells.
- 46. A method for identifying a secreted tumor antigen, comprising the steps of:

or

or

- (a) implanting tumor cells in an immunodeficient mammal;
- (b) obtaining serum from the immunodeficient mammal after a time sufficient to permit secretion of tumor antigens into the serum;
 - (c) immunizing an immunocompetent mammal with the serum;
 - (d) obtaining antiserum from the immunocompetent mammal; and
- (e) screening a tumor expression library with the antiserum, and therefrom identifying a secreted tumor antigen.
- 47. A method according to claim 46, wherein the immunodeficient mammal is a SCID mouse and wherein the immunocompetent mammal is an immunocompetent mouse.
- 48. A method for identifying a secreted ovarian carcinoma antigen, comprising the steps of:
 - (a) implanting ovarian carcinoma cells in a SCID mouse;
- (b) obtaining serum from the SCID mouse after a time sufficient to permit secretion of ovarian carcinoma antigens into the serum;
 - (c) immunizing an immunocompetent mouse with the serum;
 - (d) obtaining antiserum from the immunocompetent mouse; and
- (e) screening an ovarian carcinoma expression library with the antiserum, and therefrom identifying a secreted ovarian carcinoma antigen.
- 49. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with a binding agent that binds to an ovarian carcinoma protein, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
 - (ii) complements of the foregoing polynucleotides;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.
- 50. A method according to claim 49, wherein the binding agent is an antibody.
- 51. A method according to claim 50, wherein the antibody is a monoclonal antibody.
 - 52. A method according to claim 49, wherein the cancer is ovarian cancer.
- 53. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to an ovarian carcinoma protein, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
 - (ii) complements of the foregoing polynucleotides;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

- (d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
- 54. A method according to claim 53, wherein the binding agent is an antibody.
- 55. A method according to claim 54, wherein the antibody is a monoclonal antibody.
 - 56. A method according to claim 53, wherein the cancer is ovarian cancer.
- 57. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes an ovarian carcinoma protein, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
 - (ii) complements of the foregoing polynucleotides;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
- (c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.
- 58. A method according to claim 57, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

- 59. A method according to claim 57, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.
- 60. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes an ovarian carcinoma protein, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
 - (ii) complements of the foregoing polynucleotides;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
- 61. A method according to claim 60, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.
- 62. A method according to claim 60, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.
 - 63. A diagnostic kit, comprising:
- (a) one or more antibodies or antigen-binding fragments thereof that specifically bind to an ovarian carcinoma protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
 - (ii) complements of the foregoing polynucleotides.; and
 - (b) a detection reagent comprising a reporter group.
- 64. A kit according to claim 63, wherein the antibodies are immobilized on a solid support.
- 65. A kit according to claim 63, wherein the solid support comprises nitrocellulose, latex or a plastic material.
- 66. A kit according to claim 63, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.
- 67. A kit according to claim 63, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.
 - 68. A diagnostic kit, comprising:
- (a) an oligonucleotide comprising 10 to 40 nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes an ovarian carcinoma protein, wherein the ovarian carcinoma protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-387 or 391; and
 - (ii) complements of the foregoing polynucleotides; and
- (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

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cttaatttaa gctttctaga aagctttgga agtttttgta gatagtagaa aggggggcat
                                                                       540
cacntgagaa agagctgatt ttgtatttca ggtttgaaaa gaaataactg aacatatttt
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ttaggcaagt cagaaagaga acatggtcac ccaaaagcaa ctgtaactca gaaattaagt
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tactcagaaa ttaagtagct cagaaattaa gaaagaatgg tataatgaac ccccatatac
                                                                       720
ccttccttct ggattcacca attgttaaca ttttttcct ctcagctatc cttctaattt
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ctctctaatt tcaatttgtt tatatttacc tctgggctca ataagggcat ctgtgcagaa
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atttggaagc catttagaaa atcttttgga ttttcctgtg gtttatggca atatgaatgg
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agcttattac tggggtgagg gacagcttac tccatttgac cagattgttt ggctaacaca
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tcccgaagaa tgattttgtc aggaattatt gttatttaat aaatatttca ggatattttt
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cctctacaat aaagtaacaa t
                                                                      1041
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cagcagggcc tcatcacact gggctggatt catactcacc ccacacagac cgcgtttctc
                                                                       180
tocagtgtcg acctacacac tcactgctct taccagatga tgttgccaga gtcagtagcc
                                                                       240
attgtttgct cccccaagtt ccaggaaact ggattcttta aactaactga ccatggacta
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gaggagattt cttcctgtcg ccagaaagga tttcatccac acagcaagga tccacctctg
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ttctgtagct gcagccacgt gactgttgtg gacagagcag tgaccatcac agaccttcga
                                                                       420
tgagcgtttg agtccaacac cttccaagaa caacaaaacc atatcagtgt actgtagccc
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cacctgagaa agagctgatt ttgtatttca ggtttgaaaa gaaataactg aacatatttt
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ttaggcaagt cagaaagaga acatggtcac ccaaaagcaa ctgtaactca gaaattaagt
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tactcagaaa ttaagtagct cagaaattaa gaaagaatgg tataatgaac ccccatatac
                                                                       720
cetteettet ggatteacca attgttaaca tttttteet eteagetate ettetaattt
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ctctctaatt tcaatttgtt tatatttacc tctgggctca ataagggcat ctgtgcagaa
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atttggaage catttagaaa atettttgga ttttcctgtg gtttatggca atatgaatgg
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agcttattac tggggtgagg gacagcttac tccatttgac cagattgttt ggctaacaca
                                                                       960
tcccgaagaa tgattttgtc aggaattatt gttatttaat aaatatttca ggatattttt
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cctctacaat aaagtaacaa tta
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                                                                       120
ttgaatggga actgtttggg tttagggcat cttagagttg attgatggaa aaagcagaca
                                                                       180
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ggaactggtg ggaggtcaag tggggaagtt ggtgaatgtg gaataactta cctttgtgct
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ccacttaaac cagatgtgtt gcagctttcc tgacatgcaa ggatctactt taattccaca
                                                                       300
ctctcattaa taaattgaat aaaagggaat gttttggcac ctgatataat ctgccagget
                                                                       360
atgtgacagt aggaaggaat ggtttcccct aacaagccca atgcactggt ctgactttat
                                                                       420
aaattattta ataaaatgaa ctattatc
                                                                       448
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      <211> 411
      <212> DNA
      <213> Homo sapien
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                                                                       120
atcagtatct cagagggctc taaggtgcca agaagtctca ctggacattt aagtgccaac
                                                                       180
aaaggcatac tttcggaatc gccaagtcaa aactttctaa cttctgtctc tctcaqagac
                                                                      240
aagtgagact caagagtcta ctgctttagt ggcaactaca gaaaactggt gttacccaga
                                                                       300
aaaacaggag caattagaaa tggttccaat atttcaaagc tccgcaaaca ggatgtgctt
                                                                       360
tcctttgccc atttagggtt tcttctcttt cctttctctt tattaaccac t
                                                                       411
      <210> 22
      <211> 896
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(896)
      <223> n = A, T, C or G
      <400> 22
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gcatctcaac caccagcctc tgtggggggc aggtgggcgt ccctgtgggc ctctgggccc
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acgtccagcc tetgtcctct gccttccgtt ettcgacagt gttcccggca tccctggtca
                                                                     180
cttggtactt ggcgtgggcc tcctgtgctg ctccagcagc tcctccaggn ggtcggcccg
                                                                     240
cttcaccgca gcctcatgtt gtgtccggag gctgctcacg gcctcctcct tcctcgcgag
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ggctgtcttc accctccggn gcacctcctc cagctccagc tgctggcggg cctgcagcgt
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ggccagctcg gccttggcct gccgcgtctc ctcctcarag gctgccagcc ggtcctcgaa
                                                                      420
ctcctggcgg atcacctggg ccaggttgct gcgctcgcta gaaagctgct cgttcaccgc
                                                                      480
ctgcgcatcc tccagcgccc gctccttctg ccgcacaagg ccctgcagac gcagattctc
                                                                      540
geceteggee tecceaaget ggecetteag etecgageae egeteetgaa getteegete
                                                                      600
cgactgctcc agctcggaga gctcggcctc gtacttgtcc cgtaagcgct tgatgcggct
                                                                      660
ctcggcagcc tictcactct cctccttggc cagcgccatg tcggcctcca gccggtgaat
                                                                      720
gaccagetea ateteettgt eceggeettt eeggatttet teeeteaget eetgtteeeg
                                                                      780
gttcagcage caegeeteet eetteetggt geggeeggee teccaegeet geeteteeag
                                                                      840
ctccagctgc tgcttcaggg tattcagctc catctggcgg gcctgcagcq tggcca
                                                                      896
      <210> 23
      <211> 111
      <212> DNA
      <213> Homo sapien
      <400> 23
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attttcctag tggtttgact ttaaaaataa ataaggttta attttctccc c
                                                                      111
```

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<210> 24
      <211> 531
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(531)
      <223> n = A, T, C or G
      <400> 24
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ggctggagtg caatggtgtg atcttggctc actgcaacct ccacctcctg ggttcaagcg
                                                                       120
attetectge cacageetee egagtagetg ggattacagg tgeeegeeae cacaeeeage
                                                                       180
taatttttat atttttagta aagacagggt ttccccatgt tggccaggct ggtcttgaac
                                                                       240
ttetgacete aggtgateea eetgeetegg eeteccaaag tgttgggatt acaggegtga
                                                                       300
gctacccgtg cctggccagc cactggagtt taaaggacag tcatgttggc tccagcctaa
                                                                       360
ggcggcattt tececcatea gaaageeege ggeteetgta eeteaaaata gggcaeetgt
                                                                       420
aaagtcagtc agtgaagtct ctgctctaac tggccacccg gggccattgg cntctgacac
                                                                       480
ageettgeea ggangeetge atetgeaaaa gaaaagttea etteettee g
                                                                       531
      <210> 25
      <211> 471
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(471)
      <223> n = A, T, C or G
      <400> 25
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ccctgaatca ttgagaaaag gcggcggtgg cgacagcggc gacctaggga tcgatctgga
                                                                       120
gggacttggg gagcgtgcag agacctctag ctcgagcgcg agggacctcc cgccgggatg
                                                                       180
cctggggagc agatggaccc tactggaagt cagttggatt cagatttctc tcagcaagat
                                                                       240
actccttgcc tgataattga agattctcag cctgaaagcc aggttctaga ggatgattct
                                                                       300
ggttctcact tcagtatgct atctcgacac cttcctaatc tccagacgca caaagaaaat
                                                                       360
cctgtgttgg atgttgngtc caatccttga acaaacagct ggagaagaac gaggagaccg
                                                                       420
gtaatagtgg gttcaatgaa catttgaaag aaaaccaggt tgcaqaccct q
                                                                       471
      <210> 26
      <211> 541
      <212> DNA
      <213> Homo sapien
      <400> 26
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gagtggaagc caaagaacac ccaccttcct cccttgaagg agtagagcaa ccatcagaag
                                                                       120
atactgtttt attgctctgg tcaaacaagt cttcctgagt tgacaaaacc tcaggctctg
                                                                       180
gtgacttctg aatctgcagt ccactttcca taagttcttg tgcagacaac tgttcttttg
                                                                       240
cttccatagc agcaacagat gctttggggc taaaaggcat gtcctctgac cttqcaggtg
                                                                       300
gtggattttg ctcttttaca acatgtacat ccttactggg ctgtgctgtc acagggatgt
                                                                       360
ccttgctgga ctgttctgct atggggatat cttcgttgga ctgttcttca tgcttaattg
                                                                       420
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```
cagtattagc atccacatca gacagcctgg tataaccaga gttggtggtt actgattgta
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gctgctcttt gtccacttca tatggcacaa gtattttcct caacatcctg gctctgggaa
                                                                        540
                                                                        541
      <210> 27
      <211> 461
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(461)
      \langle 223 \rangle n = A, T, C or G
      <400> 27
gaaatgtata tttaatcatt ctcttgaacg atcagaactc traaatcagt tttctataac
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arcatgtaat acagtcaccg tggctccaag gtccaggaag gcagtggtta acacatgaag
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agtgtgggaa gggggctgga aacaaagtat tcttttcctt caaagcttca ttcctcaagg
                                                                        180
cctcaattca agcagtcatt gtccttgctt tcaaaagtct gtgtgtgctt catggaaggt
                                                                        240
atatgtttgt tgccttaatt tgaattgtgg ccaggaaggg tctggagatc taaattcaga
                                                                        300
gtaagaaaac ctgagctaga actcaggcat ttctcttaca gaacttggct tgcagggtag
                                                                        360
aatgaangga aagaaactta gaagctcaac aagctgaaga taatcccatc aggcatttcc
                                                                        420
cataggeett geaactetgt teactgagag atgttateet g
                                                                        461
      <210> 28
      <211> 541
      <212> DNA
      <213> Homo sapien
      <400> 28
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                                                                         60
tatgaacaag ataaatctat cttcaaagac atattagaag ttgggaaaat aattcatgtg
                                                                        120
aactagacaa gtgtgttaag agtgataagt aaaatgcacg tggagacaag tgcatcccca
                                                                        180
gatctcaggg acctcccct gectgtcacc tggggagtga gaggacagga tagtgcatgt
                                                                        240
tctttgtctc tgaattttta gttatatgtg ctgtaatgtt gctctgagga agcccctgga
                                                                        300
aagtctatcc caacatatcc acatcttata ttccacaaat taagctgtag tatgtaccct
                                                                        360
aagacgctgc taattgactg ccacttcgca actcaggggc ggctgcattt tagtaatggg
                                                                        420
tcaaatgatt cactttttat gatgcttccc aaggtgcctt ggcttctctt cccaactgac
                                                                        480
aaatgcccaa gttgagaaaa atgatcataa ttttagcata aaccgagcaa tcggcgaccc
                                                                        540
                                                                        541
      <210> :29
      <211> 411
      <212> DNA
      <213> Homo sapien
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agtgtatttc ttacactctg tatctatcac cagaagctga ggtgatagcc cgcttgtcat
                                                                        120
tgtcatccat attctgggac tcaggcggga actttctgga atattgccag ggagcatggc
                                                                        180
agaggggcac agtgcattct gggggaatgc acattggctc agcctgggta atgagtgata
                                                                        240
tacattacct ctgttcacaa ctcattgccc agcaccagtc acaaggcccc accaaatacc
                                                                        300
agageceaag aaatgtagte etgttgatat ggttttgetg tgtcecaace caaateteat
                                                                        360
cttgaattgt aagctcccat aattcccatg tgttgtggga gggacctggt g
                                                                        411
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<210> 30
      <211> 511
      <212> DNA
      <213> Homo sapien
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tgctttgaag atactacctg agactgggta atttataaac aaaagagatt taattgactc
                                                                       120
acagttetge atggetgaag aggeeteagg aaaettaeag teatggtgga aggeaaagga
                                                                       180
ggagcaaggc atgtcttaca tgtcagtagg agagagagcg agagcaggag aacctgccac
                                                                       240
ttataaacca ttcagatctc ataactccct atcatgagaa aaacatggag gaaaccacc
                                                                       300
teatgateca ateacetece gecaggtece teectegaca egtggggatt ataatteagg
                                                                       360
attagaggga cacagagaca aaccatatca tcattcatga gaaatccacc ctcatagtcc
                                                                       420
aatcagetee taccaggeee cacetecaac actggggatt geaattcaac atgagatttg
                                                                       480
gatggggaca cagattcaaa ccatatcata c
                                                                       511
      <210> 31
      <211> 827
      <212> DNA
      <213> Homo sapien
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ctaccagett teetgatttt eeegtttggt ceatgtgaag agetaccaeg ageeceagee
                                                                       120
tcacagtgtc cactcaaggg cagcttggtc ctcttgtcct gcagaggcag gctggtgtga
                                                                       180
ccctgggaac ttgacccggg aacaacaggt ggcccagagt gagtgtggcc tggccctca
                                                                       240
acctagtgtc cgtcctcctc tctcctggag ccagtcttga gtttaaaggc attaagtgtt
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agatacaagc teettgtgge tggaaaaaca eeeetetget gataaagete agggggeact
                                                                       360
gaggaagcag aggccccttg ggggtgccct cctgaagaga gcgtcaggcc atcagctctg
                                                                       420
tecetetggt geteceacgt etgtteetea ecetecatet etgggageag etgeacetga
                                                                       480
                                                                       540
ctggccacgc gggggcagtg gaggcacagg ctcagggtgg ccgggctacc tggcacccta
                                                                       600
tggcttacaa agtagagttg gcccagtttc cttccacctg aggggagcac tctgactcct
aacagtotto ottgooctgo catcatotgg ggtggctggo tgtcaagaaa ggccgggcat
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gctttctaaa cacagccaca ggaggcttgt agggcatctt ccaggtgggg aaacagtctt
                                                                       720
agataagtaa ggtgacttgc ctaaggcctc ccagcaccct tgatcttgga gtctcacagc
                                                                       780
                                                                       827
agactgcatg tsaacaactg gaaccgaaaa catgcctcag tataaaa
      <210> 32
      <211> 291
      <212> DNA
      <213> Homo sapien
      <400> 32
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ttggatgacc tctagagaaa ttgcccaaga agcccacctt ctggtcccaa cctgcagacc
                                                                       120
ccacagcagt cagttggtca ggccctgctg tagaaggtca cttggctcca ttgcctgctt
                                                                       180
ccaaccaatg ggcaggagag aaggccttta tttctcgccc acccattctc ctgtaccagc
                                                                       240
acctccgttt tcagtcagyg ttgtccagca acggtaccgt ttacacagtc a
                                                                       291
      <210> 33
      <211> 491
      <212> DNA
      <213> Homo sapien
      <400> 33
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tgcatgtagt tttatttatg tgttttsgtc tggaaaacca agtgtcccag cagcatgact
                                                                        60
gaacatcact cacttcccct acttgatcta caaggccaac gccgagagcc cagaccagga
                                                                       120
ttccaaacac actgcacgag aatattgtgg atccgctgtc aggtaagtgt ccgtcactga
                                                                       180
cccaracget gttacgtggc acatgactgt acagtgccac gtaacagcac tgtacttttc
                                                                       240
teccatgaac agttacetge catgtateta catgatteag aacattttga acagttaatt
                                                                       300
ctgacacttg aataatccca tcaaaaaccg taaaatcact ttgatgtttg taacgacaac
                                                                       360
atagcatcac tttacgacag aatcatctgg aaaaacagaa caacgaatac atacatctta
                                                                       420
aaaaatgctg gggtgggcca ggcacagctt cacgcctgta atcccagcac tttgggaggc
                                                                       480
ttaagcgggt g
                                                                       491
      <210> 34
      <211> 521
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(521)
      <223> n = A, T, C or G
      <400> 34
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                                                                        60
agcagaggaa gcagaagaag cggcagagtg tgtcgggcct gcacagatac cttcacttgc
                                                                       120
tggatggaaa tgaaaattac ccgtgtcttg tggatgcaga cggtgatgtg atttccttcc
                                                                     77.180
caccaataac caacagtgag aagacaaagg ttaagaaaac gacttctgat ttgtttttgg
                                                                      240
aagtaacaag tgccaccagt ctgcagattt gcaaggatgt catggatgcc ctcattctga
                                                                       300
aaatggcaag aaatgaaaaa gtacacttta gaaaataaag aggaaggatc actctcagat
                                                                       360
actgaagccg atgcagtctc tggacaactt ccagatccca caacgaatcc cagtgctgga
                                                                       420
aaggacgggc ccttccttct ggtggtggaa cangtcccgg tggtggatct tggaanggaa
                                                                       480
cctgaangtg gtgtaccccg tccaaggccg accttggcca c
                                                                       521
      <210> 35
      <211> 161
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(161)
    <223> n = A,T,C or G
      <400> 35
tecegegete geagggeneg tgecacetge cygteegeec getegetege tegecegeeg
                                                                        60
egeogetty egacegyea geatgetyee gagagtggge tycecegege tycegetyee
                                                                       120
gccgccgccg ctgctgccgc tgctgccgct gctgctgctg c
                                                                       161
      <210> 36
      <211> 341
      <212> DNA
      <213> Homo sapien
      <400> 36
ggcgggtagg catggaactg agaagaacga agaagctttc agactacgtg gggaagaatg
                                                                        60
aaaaaaccaa aattatcgcc aagattcagc aaaggggaca gggagctcca gcccgagagc
                                                                       120
ctattattag cagtgaggag cagaagcagc tgatgctgta ctatcacaga agacaagagg
                                                                       180
```

```
agctcaagag attggaagaa aatgatgatg atgcctattt aaactcacca tgggcggata
                                                                       240
acactgcttt gaaaagacat tttcatggag tgaaagacat aaagtggaga ccaagatgaa
                                                                       300
gttcaccage tgatgacact tecaaagaga ttagetcace t
                                                                       341
      <210> 37
      <211> 521
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(521)
      <223> n = A, T, C or G
      <400> 37
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                                                                        60
gtttgagatt aaatgagata atacatgtaa aattatgtgc ctggcataca gcaagattgt
                                                                       120
tgttgttgtt gatgatgatg atgatgatga taatatttt ctatccccag tgcacaactg
                                                                       180
cttgaaccta ttagataatc aatacatgtt tcttgaactg agatcaattt ccccatgttg
                                                                       240
tctgactgat gaagccctac attttcttct agaggagatg acatttgagc aagatcttaa
                                                                       300
agaaaatcag atgccttcac ctgaccactg cttggtgatc ccatggcact ttgtacatct
                                                                       360
ctccattage teteatetea ecageceate attattgtat gtgetgeett etgaagettg
                                                                       420
cagctggcta ccatcmggta gaataaaaat catcctttca taaaatagtg accctccttt
                                                                       480
tttatttgca tttcccaaag ccaagcaccg tggganggta g
                                                                       521
      <210> 38
      <211> 461
      <212> DNA
      <213> Homo sapien
      <400> 38
tatgaagaag ggaaaagaag ataatttgtg aaagaaatgg gtccagttac tagtctttga
                                                                        60
aaagggtcag tctgtagctc ttcttaatga gaataggcag ctttcagttg ctcagggtca
                                                                       120
gattteetta gtggtgtate taatcacagg aaacatetgt ggtteeetee agtetettte
                                                                       180
tgggggactt gggcccactt ctcatttcat ttaattagag gaaatagaac tcaaagtaca
                                                                       240
atttactgtt gtttaacaat gccacaaaga catggttggg agctatttct tgatttgtgt
                                                                       300
aaaatgctgt ttttgtgtgc tcataatggt tccaaaaatt gggtgctggc caaagagaga
                                                                       360
tactgttaca gaagccagca agaagacctc tgttcattca caccccggg gatatcagga
                                                                       420
attgactcca gtgtgtgcaa atccagtttg gcctatcttc t
                                                                       461
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gatgtcgcct tttcttcttc ttgctttttc tgatgttctg ctcagcatgt tctgggtgct
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teteatetge ateatteett teagatgetg tagettette eteetette tgeeteettt
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ggcctttgag acgagccagg aaggcctgct cctgggcctc taggcgagca agcttggcct
                                                                       360
tcattgtgat cccaagacgg gcagccttgt gtgctgttcg cccctcacag gcttggagca
                                                                       420
gcatctcatc agtcagaatc tttggggact tggacccctg gttgtcgtca tcactgcagc
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tctccaagtc tttgtttggc ttctctccac ctgaagtcaa tgtagccatc ttcacaaact
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tetgatacag caagttggge ttgggatgat tataacgggt ggteteetta gaaaggetee
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ttatctgtac tccatcctgc ccagtttcca ctaccaagtt ggccgcagtc ttgttgaaga
                                                                       660
gctcattcca ccagtggttt gtgaactcct tggcagggtc atgtcctacc ccatgagtgt
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atctacttta attccacact ctcattaata aattgaataa aagggaatgt tttggcacct
                                                                      300
gatataatct gccaggctat gtgacagtag gaaggaatgg tttcccctaa caagcccaat
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      <212> DNA
      <213> Homo sapien
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gtctctgcaa gtggagccag agtggaggaa tgagctctga agacacagca cccagccttc
                                                                      180
tegeaceage caageettaa etgeetgeet gaeeetgaac cagaaceeag etgaactgee
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cctccaaggg acaggaaggc tggggggggg agtttacaac ccaagccatt ccacccctc
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ctatattcct ggctctgtgt ttccgagact gcttttaatc ccaacttctc tacatttaga
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aatcctgata ggttctttat tttttcaaaa tatatttgcc atgggatgct aatttgcaat
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                                                                       540
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      <212> DNA
      <213> Homo sapien
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aactcctcaa tettgeetge ceectagtat gaageeeeet teetgeeeet acaatteetg
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```
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      <212> DNA
      <213> Homo sapien
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      <221> misc feature
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cccgtgccag gtacttcacg caecaagctc a
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      <210> 49
      <211> 511
      <212> DNA
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      <400> 49
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aatcaaaacc atttactctg ctaactcatt attttttgct ttctttttgg ttaagagagg
                                                                       240
caatgcaata cactgaaaaa ggtttttatc ttatctggca ttggaattag acatattcaa
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<213> Homo sapien
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caagaggttc tgcagaactt catggagcat gaaagtaaat aaacaaagtt aatttcaagg
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gaattttggc caggcatggt g
                                                                       561
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tatttctatg caaaagtatg ccttcaaact gcttaaatga tatatgatat gatacacaaa
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aagacacctt acacacacac acacacacac acacacacgt gtgcaccgcc aatgacaaaa
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                                                                        540
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ctcttccaca tcctcacata gaccccagac ccgctggccc ctggctgggc atcgcattgc
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tettttavag ccatcattta aagemggntt etetecaaca egagtetget sasggggggk
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      <211> 561
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gagagactcg taagtgcaga aaacatggtc cagcetttgt tcatggctcc agcetcacag
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                                                                       561
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      <211> 811
      <212> DNA
      <213> Homo sapien
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      <220>
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cgtgccccan gagcttccca cctgctgctg gctccctggg tggctttggg aacagcttgg
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attttttctg tattaaacct ctatcatagt ttaagcctat tagggtactt aatccttaca
                                                                       240
aataaacagg tttaaaatca cctcaatagg caactgccct tctggttttc ttctttgact
                                                                       300
aaacaatctg aatgcttaag attttccact ttgggtgcta gcagtacaca gtgttacact
                                                                       360
                                                                       420
ctgtattcca gacttcttaa attatagaaa aaggaatgta cactttttgt attctttctg
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      <210> 58
      <211> 141
      <212> DNA
      <213> Homo sapien
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                                                                       120
caccatgccc agctaatttt t
                                                                       141
      <210> 59
      <211> 191
      <212> DNA
      <213> Homo sapien
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ccttacaagt gtaatgagtg tggcaaagcc tttggcaagc agtcaacact tattcaccat
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PCT/US99/30270

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<212> DNA

<213> Homo sapien

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caaccccctc gcctgccctg ccetccatca ggaggagcca gtggaacctt cggaaagctc
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ccaqcatctc agcagccctc aaaagtcgtc ctggggcaag ctctggttct cctgactgga
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                                                                     120
gcttaactga aatagcgtcc atccaaaagt gggtttaagg taaaactacc tgacgatatt
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ggcggggatc ctgcagtttg gactgcttgc cgggtttgtc caggqttccq qqtctqttct
                                                                     240
tggcactcat ggggacaggc atcetgctcg tctgtggggc cccgctggag cccttacgtg
                                                                     300
aagctgaagg tatcgaccst agggggctct agggcagtgg gaccttcatc cqqaactaac
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                                                                     394
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      <211> 359
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atttttccat gaagatgtac ggaaatctga tgttgaatat gaaaatggcc cccaaatgga
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attccaaaag gttaccacag gggctgtaag acctagtgac cctcctaagt gggaaagagg
                                                                     240
aatggagaat agtatttctg atgcatcaag aacatcagaa tataaaactg agatcataat
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cttatagagt ggaggaggca aacaggtccc ctcaatgtac cagatggtca cctatagcac
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actgnetttt ggatgetete ttgggeeacg
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ccggaggggc agcaaccccc cgcacacgtc agccaacagc agtqcctctq cagqcaccaa
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gagagcgatg atggacttga gcgccgtgtt c
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gaggttaggg cccccaggcg ggctaagtgc tattggcctg ctcctgctca aagagagcca
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tagecagetg ggeaeggeee eetageeeet ceaggttget gaggeggeag eggtggtaga
                                                                       240
gttcttcact gagccgtggg ctgcagtctc gcagggagaa cttctgcacc agccctggct
                                                                       300
ctacggcccg aaagaggtgg agecctgaga accggaggaa aacatccatc acctccaqcc
                                                                       360
ectecaggge ttectectet teetggeetg ceagtteace tgecageegg getegggeeg
                                                                       420
ccaggtagtc agcgttgtag aagcagccct ccgcagaagc ctgccggtca aatctccccg
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gattagcaag ggacccctca ctaagtgttg atggagttag gacagagctc agctgtttga
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atctcagage ccaggeaget ggagetgggt aggateetgg agetggeact aatgtgaggt
                                                                        360
gcattecete caacecagge teagateegg aacetgaceg tgetgaceee egaaggggag
                                                                        420
gcagggctga gctggcccgt tgggctccct gctcctttca caccacactc tcgctttgag
                                                                        480
gtgctgggct gggactactt cacagagcag c
                                                                        511
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                                                                       120
geceetggag gagatetgge etetetgtga ttteateact gtgeacaete eteteetgee
                                                                       180
ctccacgaca ggcttgctga atgacaacac ctttgcccag tgcaagaagg gggtgcgtgt
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ggtgaactgt gcccgtggag ggatcgtgga cgaaggcgcc ctgctccggg ccctgcagtc
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tggccagtgt gccggggctg cactggacgt gtttacggaa gagccgccac gggaccgggc
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tcagagccgc tgtggggagg aaattgctgt tcagttcgtg gacatggtga aggggaaatc
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aacagtttga taacctcaaa ccttcaggag gttacataac aggtgatcaa gcccgtactt
                                                                       180
ttttcctaca gtcaggtctg ccggccccgg ttttagctga aatatgggcc ttatcagatc
                                                                       240
tgaacaagga tgggaagatg gaccagcaag agttctctat agctatgaaa ctcatcaagt
                                                                       300
taaagttgca gggccaacag ctgcctgtag tcctccctcc tatcatgaaa caacccccta
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atcagccatt gcctccagtt gcacctatag caacaccctt gtcttctgct acttcaggga
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tgectcatge atcatettae agectgatga tgggaggatt tggtggtget agtatecaga
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ggaaagccaa ctatgaacga ggaaacatgg agctggagaa gcgacgccaa gtgttgatgg
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ggcaggagct gctcagtcag aagaccaggg aacaagaaga cattgtcagg ctgagctcca
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ataaacagtg tgacctggaa attatggaaa tcaaacaact tcaacaagag cttaaggaat
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aaaaggaaga attatgccaa agacttaaag aacaattaga tgctcttgaa aaagaaactg
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ataatacaca gcagttagcc cttgaacaac ttcataaaat caaacgtgac aaattgaagg
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taatcagtat ctcagagggc tctaaggtgc caagaagtct cactggacat ttaagtgcca
                                                                       180
acaaaggcat acttteggaa tegecaagte aaaaetttet aaettetgte teteteagag
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acaagtgaga ctcaagagtc tactgcttta gtggcaacta cagaaaactg gtgttaccca
                                                                       300
gaaaaacagg agcaattaga aatggttcca atatttcaaa gctccgcaaa caggatgtgc
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gcccctggaa agtctatccc aacatatcca catcttatat tccacaaatt aagctgtagt
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cattetacce tgcaagccaa gttetgtaag agaaatgeet gagttetage teaggtttte
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atatacette catgaageae acacagaett ttgaaageaa ggacaatgae tgettgaatt
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cactetteat gtgttaacca etgeetteet ggaeettgga geeaeggtga etgtattaca
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tgttgttata gaaaactgat tttagagttc tgatcgttca agagaatgat taaatataca
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ggaagacctg ggggaaaaca ccatggtttt atccaccctg agatctttga acaacttcat
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ctctcagcgt gcggagggag gctctggact ggatatttct acctcggccg cgaccacgct
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      <211> 330
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      <223> n = A, T, C or G
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                                                                      120
tcagcctgca gccagagtac agagggccaa cactggtgtt cttgaacaag ggccttagca
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ggccctgaag grccctctct gtagtgttga acttcctgga gccaggccac atgttctcct
                                                                      240
cataccgcag gytagygatg gtgaagttga gggtgaaata gtattmangr agatggctgg
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caracetgee egggeggeeg etesaaatee
                                                                      330
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cagecaccag agtggatget gtetgeacce ategteetga ecceaaaage eetggactgg
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acagagageg getgtaetgg aagetgagee agetgaeeea eggeateaet gagetgggee
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cctacaccct ggacagggac agtctctatg tcaatggttt cacccatcgg agctctgtac
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ccaccaccag caccggggtg gtcagcgagg agccattcaa cctgcccggg cggccgctcg
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      <211> 356
      <212> DNA
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              <223> n = A, T, C or G
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                                                                                                                                                   120
 gaagttcaac accacggaga gggtccttca gggcctgctc aggtccctgt tcaagagcac
                                                                                                                                                   180
 cagigting contended to contend the cagacter against cagacter against against cagacters against a cagacter ag
                                                                                                                                                   240
 ggcagccact ggagtggacg ccatctgcac cctccgcctt gatcccactg gtcctggact
                                                                                                                                                   300
 qqacagagag cggctatact gggagctgag ccagtcctct ggcggngacn ccnctt
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             <211> 226
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             <213> Homo sapien
             <400> 79
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                                                                                                                                                    60
 gaggaagate tetgetgtea gtgagaagge tgtcatecae tgagatggea gtcaaaagtg
                                                                                                                                                  120
 catttaatac acctaacgta tcgaacatca tagcttggcc caggttatct catatgtgct
                                                                                                                                                  180
 cagaacactt acaatageet geagacetge eegggeggee getega
                                                                                                                                                  226
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             <211> 444
             <211> 444
<212> DNA
             <213> Homo sapien
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             <221> misc feature
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             <223> n = A, T, C or G
             <400> 80
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gatggtgaag ttgagggtga atggtaccag gagagggcca gcagccataa ttgtsgrgck
                                                                                                                                                  120
gsmgmssgag gmwggwgtyy cwgaggttcy rarrtccact gtggaggtcc caggagtgct
                                                                                                                                                  180
ggtggtgggc acagagstcy gatgggtgaa accattgaca tagagactgt tcctgtccag
                                                                                                                                                  240
ggtgtagggg cccagctctt yratgycatt ggycagttkg ctyagctccc agtacagccr
                                                                                                                                                  300
ctctckgyyg mgwccagsgc ttttggggtc aagatgatgg atgcagatgg catccactcc
                                                                                                                                                  360
agtggctgct ccatccttct cggacctgag agaggtcagt ctgcagccag agtacagagg
                                                                                                                                                  420
gccaacactg gtgttctttg aata
                                                                                                                                                  444
            <210> 81
            <211> 310
            <212> DNA
            <213> Homo sapien
            <400> 81
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                                                                                                                                                    60
ttccacctgt gctgcggaca tctccaggga gtgcagaagg gaagcaggtc aaactgctca
                                                                                                                                                  120
gatcagtcag actggctgtt ctcagttctc acctgagcaa ggtcagtctg cagccagagt
                                                                                                                                                 180
acagagggcc aacactggtg ttcttgaaca agggcttgag cagaccctgc agaaccctct
                                                                                                                                                  240
teegtggtgt tgaactteet ggaaaccagg gtgttgeatg ttttteetea taatgeaagg
                                                                                                                                                  300
ttggtgatgg
                                                                                                                                                  310
```

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<210> 82
       <211> 571
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(571)
       <223> n = A, T, C or G
       <400> 82
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 tacaaatgga atttcatctt gtttccatgc tgagtagtga aacagtgaca aagctaatca
                                                                        120
 taataaccta catcaaaaga gaactaagct aacactgctc actttcttt taacaggcaa
                                                                        180
aatataaata tatgcactct anaatgcaca atggtttagt cactaaaaaa ttcaaatggg
                                                                        240
atcttgaaga atgtatgcaa atccagggtg cagtgaagat gagctgagat gctgtgcaac
                                                                        300
tgtttaaggg ttcctggcac tgcatctctt ggccactagc tgaatcttga catggaaggt
                                                                        360
tttagctaat gccaagtgga gatgcagaaa atgctaagtt gacttagggg ctgtgcacag
                                                                        420
gaactaaaag gcaggaaagt actaaatatt gctgagagca tccaccccag gaaggacttt
                                                                        480
accttccagg agctccaaac tggcaccacc cccagtgctc acatggctga ctttatcctc
                                                                        540
cgtgttccat ttggcacagc aagtggcagt g
                                                                        571
      <210> 83
      <211> 551
      <212> DNA
      <213> Homo sapien
      <400> 83
aaggctggtg ggtttttgat cctgctggag aacctccgct ttcatgtgga ggaagaaggg
                                                                         60
aagggaaaag atgettetgg gaacaaggtt aaagcegage eagceaaaat agaagettte
                                                                        120
cgagetteae tttccaaget aggggatgte tatgtcaatg atgettttgg cactgeteae
                                                                        180
agagcccaca gctccatggt aggagtcaat ctgccacaga aggctggtgg gtttttgatg
                                                                        240
aagaaggage tgaactactt tgcaaaggce ttggagagee cagagegace etteetggee
                                                                        300
atcctgggcg gagctaaagt tgcagacaag atccagctca tcaataatat gctggacaaa
                                                                        360
gtcaatgaga tgattattgg tggtggaatg gcttttacct tccttaaggt gctcaacaac
                                                                        420
atggagattg gcacttctct gtttgatgaa gagggagcca agattgtcaa agacctaatg
                                                                       480
tecaaagetg agaagaatgg tgtgaagatt accttgcctg ttgactttgt cactgctgac
                                                                        540
aagtttgatg a
                                                                       551
      <210> 84
      <211> 571
      <212> DNA
      <213> Homo sapien
      <400> 84
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                                                                        60
taagttctga ttccaactta gctaattcat tctgagaact gtggtatagg tggcgtgtct
                                                                       120
cttctagctg ggacaaaagt tctttgtttt ccccctgtag agtatcacag accttctgct
                                                                       180
gaagetggae ctetgtetgg geettggaet eccaaatetg ettgteatgt teaageetgg
                                                                       240
aaatgttaat ctttaattct tccatatgga tggacatctg tctaagttga tcctttagaa
                                                                       300
cactgcaatt atcttctttg agtctaattt cttcttcttt gctttgaatc gcatcactaa
                                                                       360
acttectete ecatttetta getteateta teaccetgte acgateatee tggagggaag
                                                                       420
acatgetett agtaaagget geaagetggg teacagtact gtecaagttt teetgaagtt
                                                                       480
gctgaacttc cttgtctttc ttgttcaaag taacctgaat ctctccaatt gtctcttcca
                                                                       540
```

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agtggacttt ttctctgcgc aaagcatcca g
                                                                       571
      <210> 85
      <211> 561
      <212> DNA
      <213> Homo sapien
      <400> 85
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aatcaaagga ttcagcatgt ggtggaagct gtgaggcaag agaaacaaga actgtatggc
                                                                       120
aagttaagaa gcacagaggc aaacaagaag gagacagaaa agcagttgca ggaagctgag
                                                                       180
caagaaatgg aggaaatgaa agaaaagatg agaaagtttg ctaaatctaa acagcagaaa
                                                                       240
atcctagage tggaagaaga gaatgaccgg cttagggcag aggtgcaccc tgcaggagat
                                                                       300
acagctaaag agtgtatgga aacacttctt tcttccaatg ccagcatgaa ggaagaactt
                                                                       360
gaaagggtca aaatggagta tgaaaccctt tctaagaagt ttcagtcttt aatgtctgag
                                                                       420
aaagactete taagtgaaga ggtteaagat ttaaageate agatagaagg taatgtatet
                                                                       480
aaacaagcta acctagaggc caccgagaaa catgataacc aaacgaatgt cactgaagag
                                                                       540
ggaacacagt ctataccagg t
                                                                       561
      <210> 86
      <211> 795
      <212> DNA
      <213> Homo sapien
      <400> 86
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aattctcacc gttacaacaa ccccatgagg tatttattcc cattctatag atagggaaac
                                                                      .120
cacagotoaa gtaagttagg aaactgagoo aagtatacao agaatacgaa gtggcaaaao
                                                                       180
tagaaggaaa gactgacact gctatctgct ggcctccagt gtcctggctc ttttcacacg
                                                                       240
ggttcaatgt ctccagcgct gctgctgctg ctgcattacc atgccctcat tgttttctt
                                                                       300
cctctggtgt tcaactgcat ccttcaaaga atctaactca ttccagagac cacttatttc
                                                                       360
tttctctctt tctgaaatta cttttaataa ttcttcatga gggggaaaag aagatgcctg
                                                                       420
ttggtagttt tgttgtttaa gctgctcaat ttgggactta aacaatttgt tttcatcttg
                                                                       480
tacatectgt aacagetgtg ttttgetaga aagateacte teeetetet ttageatgge
                                                                      540
ttctaacctc ttcaattcat tttccttttc tttcaacaca atctcaagtt cttcaaactg
                                                                      600
tgatgcagaa gaggcctctt tcaagrtatg ttgtgctact tcctgaacat qtqcttttaa
                                                                       660
agatteattt tettettgaa gateetgtaa ceaetteeet gtattggeta ggtetteete
                                                                      720
tttctcttcc aaaacagcct tcatggtatt catctgttcc tcttttcctt ttaataagtt
                                                                      780
caggagette agaac
                                                                      795
      <210> 87
      <211> 594
      <212> DNA
      <213> Homo sapien
      <400> 87 -
caagettttt tttttttt aaaaagtgtt ageattaatg ttttattgte aegeagatgg
                                                                       60
caactgggtt tatgtcttca tattttatat ttttgtaaat taaaaaaatt acaagtttta
                                                                      120
aatagccaat ggctggttat attttcagaa aacatgatta gactaattca ttaatggtgg
                                                                      180
cttcaagett ttccttattg gctccagaaa attcacccac cttttgtccc ttcttaaaaa
                                                                      240
actggaatgt tggcatgcat ttgacttcac actctgaagc aacatcctga cagtcatcca
                                                                      300
catctacttc aaggaatatc acgttggaat acttttcaga gagggaatga aagaaaggct
                                                                      360
tgatcatttt gcaaggccca caccacgtgg ctgagaagtc aactactaca agtttatcac
                                                                      420
ctgcagcgtc caaggettcc tgaaaagcag tettgetete gatetgette accatettgg
                                                                      480
ctgctggagt ctgacgagcg gctgtaagga ccgatggaaa tggatccaaa gcaccaaaca
                                                                      540
```

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gagetteaag actegetget tggettgaat teggateega tategeeatg geet
                                                                      594
      <210> 88
      <211> 557
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      <400> 88
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tttatatttt tgtaaattaa aaaaattmca agttttaaat agccaatggc tggttatatt
                                                                      120
ttcagaaaac atgattagac taattcatta atggtggctt caagcttttc cttattggct
                                                                      180
ccagaaaatt cacccacctt ttgtcccttc ttaaaaaact ggaatgttgg catgcatttg
                                                                      240
acttcacact ctgaagcaac atcctgacag tcatccacat ctacttcaag gaatatcacg
                                                                      300
ttggaatact tttcagagag ggaatgaaag aaaggcttga tcattttgca aggcccacac
                                                                      360
cacgtggctg agaagtcaac tactacaagt ttatcacctg cagcgtccaa ggcttcctga
                                                                       420
aaagcagtet tgetetegat etgetteace atettggetg etggagtetg acgagegget
                                                                       480
gtaaggaccg atggaaatgg atccaaagca ccaaacagag cttcaagact cgctgcttgg
                                                                      540
catgaattcg gatccga
                                                                       557
      <210> 89
      <211> 561
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(561)
      <223> n = A, T, C or G
      <400> 89
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qcacctqqcc acaqqqtcca ctqaaacqqq qaqqqqatqq caqcttqtaa tqtqqctttt
                                                                       120
                                                                       180
gccacaaccc cettetgaca gggaaggeet tagattgagg ceecacetee catggtgatg
qqqaqctcaq aatqqqqtcc aqqqaqaatt tqqttaqqqq qaqqtqctaq qqaqqcatqa
                                                                       240
                                                                       300
gcagagggca ccctccgagt ggggtcccga gggctgcaga gtcttcagta ctgtccctca
                                                                       360
cagcagetgt etcaaggetg ggteeetcaa aggggegtee cagegeggg ceteeetgeg
caaacacttg gtaccectgg ctgcgcagcg gaagccagca qgacagcagt ggcqccgatc
                                                                       420
agcacaacag acgccctggc ggtagggaca gcaggcccag ccctgtcggt tgtctcggca
                                                                       480
gcaggtctgg ttatcatggc agaagtgtcc ttcccacact tcacgtcctt cacacccacg
                                                                       540
                                                                       561
tganggctac nggccaggaa g
      <210> 90
      <211> 561
      <212> DNA
      <213> Homo sapien
      <400> 90
                                                                        60
cccgtgggtg ccatccacgg agttgttacc tgatctttgg aagcaggatc gcccgtctgc
actgcagtgg aageccegtg ggcagcagtg atggccatec cegcatgcca eggectetgg
                                                                       120
gaaggggcag caactggaag tccctgagac ggtaaagatg caggagtggc cggcagagca
                                                                       180
                                                                       240
gtgggcatca acctggcagg ggccacccag atgcctgctc agtgttgtgg gccatttgtc
cagaagggga cggcagcagc tgtagctggc tcctccgggg tccaggcagc aggccacagg
                                                                       300
gcagaactga ccatctgggc accgcgttcc agccaccagc cctgctgtta aggccaccca
                                                                       360
gctcaccagg gtccacatgg tctgcctgcg tccgactccg cggtccttgg gccctgatgg
                                                                       420
ttctacctgc tgtgagctgc ccagtgggaa gtatggctgc tgccaatgcc caacgccacc
                                                                       480
```

```
tgctgctccg atcacctgca ctgctgcccc aagacactgt gtgtgacctg atccagagta
                                                                      540
agtgcctctc caaggagaac g
                                                                      561
      <210> 91
      <211> 541
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(541)
      <223> n = A, T, C or G
      <400> 91
gaatcacctt tctggtttag ctagtacttt gtacagaaca atgaggtttc ccacagcgga
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gtctccctgg gctctgtttg gctctcggta aggcaggcct acaccttttc ctctcctcta
                                                                     120
tggagagggg aatatgcatt aaggtgaaaa gtcaccttcc aaaagtgaga aagggattcg
                                                                     180
attgctgctt caggactgtg gaattatttg gaatgtttta caaatggttg ctacaaaaca
                                                                     240
acaaaaaagg taattacaaa atgtgtacat cacaacatgc tttttaaaga cattatgcat
                                                                     300
tgtgctcaca ttcccttaaa tgttgtttcc aaaggtgctc agcctctagc ccagctggat
                                                                     360
tctccgggaa gaggcagaga cagtttggcg aaaaagacac agggaaggag ggggtggtga
                                                                     420
aaggagaaag cagcetteea gttaaagate ageeeteagt taaaggteag etteeegean
                                                                     480
getggeetea ngeggagtet gggteagagg gaggageage ageagggtgg gaetggggeg
                                                                     540
                                                                     541
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      <211> 551
      <212> DNA
      <213> Homo sapien
      <400> 92
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                                                                      60
gtgaagcgca agatccaggt tctgcagcag caggcagatg atgcagagga gcgagctgag
                                                                     120
cgcctccagc gagaagttga gggagaaagg cgggcccggg aacaggctga ggctgaggtg
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gcctccttga accgtaggat ccagctggtt gaagaagagc tggaccgtgc tcaggagcgc
                                                                     240-
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                                                                     300
ggtatgaagg ttattgaaaa cegggcetta aaagatgaag aaaagatgga actecaggaa
                                                                     360
atccaactca aagaagctaa gcacattgca gaagaggcag ataggaagta tgaagaggtg
                                                                     420
480
gcagagtccc gttgccgaga gatggatgag cagattagac tgatggacca gaacctgaag
                                                                     540
tgtctgagtg c
                                                                     551
      <210> 93
      <211> 531
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     <400> 93
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                                                                      60
gatetggttt tetggatage caggteatag catgggtate agtaggaate egetgtaget
                                                                     120
gcacaggeet caettgetge agtteegggg agaacaeetg caetgeatgg egttgatgae
                                                                     180
ctcgtggtac acgacagagc cattggtgca gtgcaagggc acgcgcatgg gctccgtcct
                                                                     240
cgagggcagg cagcaggagc attgctcctg cacatcctcg atgtcaatgg agtacacagc
                                                                     300
tttgctggca cactttccct ggcagtaatg aatgtccact tcctcttggg acttacaatc
                                                                     360
teceactitg atgractgea eetiggetgt gatgrettig caatcagget eeteacatgt
                                                                     420
```

```
gtcacagcag gtgcctggaa ttttcacgat tttgcctcct tcagccagac acttgtgttc
                                                                       480
atcaaatggt gggcagcccg tgaccctctt ctcccagatg tactctcctc t
                                                                       531
      <210> 94
      <211> 531
      <212> DNA
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      <221> misc_feature
      <222> (1)...(531)
      <223> n = A, T, C or G
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                                                                       60
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                                                                      120
teteetgtte gggtggagga gaegtgtgge tgeegetgga eetgeeettg tgtgtgeaeg
                                                                      180
ggcagttcca ctcggcacat cgtcaccttc gatgggcaga atttcaagct tactggtage
                                                                      240
tgctcctatg tcatctttca aaacaaggag caggacctgg aagtgctcct ccacaatggg
                                                                      300
qeetqeagee eeggggeaaa acaageetge atgaagteea ttgagattaa geatgetgge
                                                                      360
gtctctgctg agctgcacag taacatggag atggcagtgg atgggagact ggtccttgcc
                                                                      420
ccgtacgttg gtgaaaacat ggaagtcagc atctacggcg ctatcatgta tgaagtcagg
                                                                      480
tttacccatc ttggccacat cctcacatac accgccncaa aacaacgagt t
                                                                      531
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      <211> 605
      <212> DNA
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      <400> 95
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                                                                       60
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                                                                      120
rsgraraytt agacaycccm cctcwgagac gsagkaccar gtgcagaggt ggactctttc
                                                                      180
tggatgttgt agtcagacag ggtgggtcca tcttccagct gtttcccagc aaagatcaac
                                                                      240
ctctgctgat caggagggat gecttectta tettggatet ttgccttgac attctcgatg
                                                                      300
gtgtcactgg gctccacctc gagggtgatg gtcttaccag tcagggtctt cacgaagaty
                                                                      360
tgcatcccac ctctgagacg gagcaccagg tgcagggtrg actctttctg gatgttgtag
                                                                      420
teagacaggg tgegyeeate tteeagetge ttteesagea aagateaace tetgetggte
                                                                      480
aggaggratg cottoottgt cytggatott tgcyttgacr ttotoratgg tgtoactogg
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ctccacttcg agagtgatgg tcttaccagt cagggtcttc acgaagatct gcatcccacc
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tctaa
                                                                      605
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      <211> 531
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      <400> 96
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                                                                      120
gaggaggtga agcatctcaa acataatctc gaaaaagtgg aaggagaaag aaaagaggct
                                                                      180
caagacatgc ttaatcactc agaaaaggaa aagaataatt tagagataga tttaaactac
                                                                      240
aaacttaaat cattacaaca acggttagaa caagaggtaa atgaacacaa agtaaccaaa
                                                                      300
gctcgtttaa ctgacaaaca tcaatctatt gaagaggcaa agtctgtggc aatgtgtgag
                                                                      36Ó
atggaaaaaa agctgaaaga agaaagagaa gctcgagaga aggctgaaaa tcgggttgtt
                                                                      420
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31

```
cagattgaga aacagtgttc catgctagac gttgatctga agcaatctca gcagaaacta
                                                                       480
gaacatttga ctggaaataa agaaaggatg gaggatgaag ttaagaatct a
                                                                       531
      <210> 97
      <211> 1017
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(1017)
      <223> n = A, T, C or G
      <400> 97
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cttctcccga gtgggcagca gcaactttcg cggtggcctg ggcggcggct atggtggggc
                                                                       180
cagcggcatg ggaggcatca ccgcagttac ggtcaaccag agcctgctga gcccccttgt
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cctggaggtg gaccccaaca tccaggccgt gcgcacccag gagaaggagc agatcaagac
                                                                       300
ceteaacaac aagtttgeet eetteataga caaggtaegg tteetggage ageagaacaa
                                                                       360
gatgctggag accaagtgga gcctcctgca gcagcagaag acggctcgaa gcaacatgga
                                                                       420
caacatgttc gagagctaca tcaacarcct taggcggcag ctggagactc tgggccagga
                                                                       480
gaagctgaag ctggaggcgg agcttggcaa catgcagggg ctggtggagg acttcaagaa
                                                                       540
caagtatgag gatgagatca ataagcgtac agagatggag aacgaatttg tcctcatcaa
                                                                       600
gaaggatgtg gatgaagctt acatgaacaa ggtagagctg gagtctcgcc tggaagggct
                                                                       660
gaccgacgag atcaacttcc tcaggcagct gtatgaagag gagatccggg agctgcagtc
                                                                       720
ccagatctcg gacacatctg tggtgctgtc catggacaac agccgctccc tggacatgga
                                                                       780
caqcatcatt gctgaggtca aggcacagta cgaggatatt gccaaccgca gccgggctga
                                                                       840
ggctgagagc atgtaccagg tcaagtatga ggagctgcag agcctggctg ggaagcacgg
                                                                       900
ggatgacctg cggcgcacaa agactgagat ctctgagatg aacccggaac atcagcccgg
                                                                       960
ctncaggctg agattgaggg cctcaaaggc caganggctt ncctggangn ccgccat
                                                                      1017
      <210> 98
      <211> 561
                  . The second
      <212> DNA
      <213> Homo sapien
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agcacctgca cctggagtct acccagggcc acccagcggc cctggggcct acccatcttc
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tggacageca agtgecaceg gagectacee tgecactgge ceetatggeg ecectgetgg
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gccactgatt gtgccttata acctgccttt gcctggggga gtggtgcctc gcatgctgat
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aacaattetg ggcacggtga agcccaatge aaacagaatt getttagatt tecaaagagg
                                                                       480
gaatgatgtt gccttccact ttaacccacg cttcaatgag aacaacagga gagtcattgg
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     <400> 99
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tgttgtagtc agacagggtr cgwccatctt ccagctgttt yccrgcaaag atcaacctct
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getgateagg aggratgeet teettatett ggatetttge ettgacatte tegatggtgt
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cactgggctc cacctcgagg gtgatggtct taccagtcag ggtcttcacg aagatytgca
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tcccacctct gagacggagc accaggtgca gggtrgactc tttctggatg ttgtagtcag
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acagggtgcg yccatcttcc agctgctttc csagcaaaga tcaacctctg ctggtcagga
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ggratgcctt ccttgtcytg gatctttgcy ttgacrttct caatggtgtc actcggctcc
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acttcgagag tgatggtctt accagtcagg gtcttcacga agatctgcat cccacctcta
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agacggagca ccaggtgcag ggtggactct ttctggatgg ttgtagtcag acagggtgcg
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gaagaccctg actggtaaga ccatcactct cgaagtggag ccgagtgaca ccattgagaa
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ygtcaargca aagatccarg acaaggaagg catycctcct gaccagcaga ggttgatctt
                                                                       240
tgctsggaaa gcagctggaa gatggregca ceetgtetga etacaacate cagaaagagt
                                                                       300
cyaccetgea cetggtgete egteteagag gtgggatgea ratettegtg aagaceetga
                                                                       360
ctggtaagac catcaccctc gaggtggagc ccagtgacac catcgagaat gtcaaggcaa
                                                                       420
agatccaaga taaggaaggc atccctcctg atcagcagag gttgatcttt gctgggaaac
                                                                       480
agctggaaga tggacgcacc ctgtctgact acaacatcca gaaagagtcc acctytgcac
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ytggtmetbe gtetyagagg kgggrtgeaa atetwmgtkw agacaeteae tkkyaagryy
                                                                       600
atcamcmwtg akktcgakys castkwcact wtcrakaamg tyrwwgcawa gatccmagac
                                                                       660
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      <210> 101
      <211> 451
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      <213> Homo sapien
      <400> 101
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                                                                       120
aggcaggcgt caccataatt tttgtatttt tagtagagac atggtttcgc catgttggct
                                                                       180
gggctggtct cgaactcctg acctcaagtg atctgtcctg gcctcccaaa gtgttgggat
                                                                       240
tacaggcgaa agccaacgct cccggccagg gaacaacttt agaatgaagg aaatatgcaa
                                                                       300
aagaacatca catcaaggat caattaatta ccatctatta attactatat gtgggtaatt
                                                                       360
atgactattt cccaagcatt ctacgttgac tgcttgagaa gatgtttgtc ctgcatggtg
                                                                       420
gagagtggag aagggccagg attettaggt t
                                                                       451
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      <212> DNA
      <213> Homo sapien
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                                                                       120
ctggaggagg cagaaaaagc tgcagatgag agtgagagag gaatgaaggt gatagaaaac
                                                                       180
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cgggccatga aggatgagga gaagatggag attcaggaga tgcagctcaa agaggccaag
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                                                                       300
gagggtgagc tggagagggc agaggagcgt gcggaggtgt ctgaactaaa atgtggtgac
                                                                       360
ctggaagaag aactcaagaa tgttactaac aatctgaaat ctctggaggc tgcatctgaa
                                                                       420
aagtattctg aaaaggagga caaatatgaa gaagaaatta aacttctgtc tgacaaactg
                                                                       480
aaagaggctg agacccgtgc tgaatttgca gagagaacgg ttgcaaaact ggaaaagaca
                                                                       540
attgatgacc tggaagagaa acttgcccag c
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gaagetgtee ceteeteet geeacetee eaggeteatt agtgteettg gaaggggeag
                                                                       180
aggactcaga ggggatcagt ctccaggggc cctgggctga agcgggtgag gcagagagtc
                                                                       240
ctgaggccac agagctgggc aacctgagcc gcctctctgg cccctcccc caccactgcc
                                                                       300
caaacctgtt tacagcacct tegecectee cetetaaace egtecateca etetgeactt
                                                                       360
cccaggcagg tgggtgggcc aggcctcagc catactcctg ggcgcgggtt tcggtgagca
                                                                       420
aggcacagte ccagaggtga tatcaaggee t
                                                                       451
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acggccccca cagccggatc ccctcagcct tccaggtcct caactcccgt ggacgctgaa
                                                                       180
caatggcctc catggggcta caggtaatgg gcatcgcgct ggccgtcctg ggctggctgg
                                                                       240
cegtcatget gtgctgegeg etgcccatgt ggcgcgtgac ggccttcatc ggcagcaaca
                                                                       300
ttgtcacctc gcagaccatc tggggagggcc tatggatgaa ctgcgtggtg cagagcaccg
                                                                       360
gccagatgca gtgcaaggtg tacgactcgc tgctggcact gccgcaggac ctgcaggcqq
                                                                       420
cccgcgccct cgtcatcatc a
                                                                       441
                     * *; : .
     <210> 105
     <211> 509
     <212> DNA
     <213> Homo sapien.
     <220>
     <221> misc feature
     <222> (1)...(509)
     <223> n = A, T, C or G
     <400> 105
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ecccagetee eegaccacaa ecceetteet ecccegggga aagcaagaag gagcaggtgt
                                                                       120
ggcatctgca gctgggaaga gagaggccgg ggaggtgccg agctcggtgc tggtctcttt
                                                                       180
ccaaatataa atacntgtgt cagaactgga aaatcctcca gcacccacca cccaaqcact
                                                                       240
ctccgttttc tgccggtgtt tggagagggg cggggggcag gggcgccagg caccggctgg
                                                                       300
ctgcggtcta ctgcatccgc tgggtgtgca ccccgcgagc ctcctgctgc tcattgtaga
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agagatgaca ctcggggtcc ccccggatgg tgggggctcc ctggatcagc ttcccggtgt
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tggggttcac acaccagcac tccccacgct gcccgttcag agacatcttg cactgtttga
                                                                     480
ggttgtacag gccatgcttg tcacagttg
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giacatttta agccaataag ctgcaggatg tacacctaac agacctccta gaaaccttac
                                                                     180
cagaaaatgg ggactgggta gggaaggaaa :cttaaaagat caacaaactg ccagcccacg
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tttcaaaata atataaaatt taaaaagttt tgtacataag ctattcaaga tttctccagc
                                                                     360
actgactgat acaaagcaca attgagatgg cacttctaga gacagcagct tcaaacccag
                                                                     420
aaaagggtga tgagatgagt ttcacatggc taaatcagtg gcaaaaacac agtcttcttt
                                                                     480
ctttctttct ttcaaggagg caggaaagca attaagtggt cacctcaaca taagggggac
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     <211> 555
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tgagcgcctc cagcgagaag ttgagggaga aaggcgggcc cgggaacagg ctgagqctga
                                                                     180
ggtggcctcc ttgaaccgta ggatccagct ggttgaagaa gagctggacc gtgctcagga
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gcgcctggcc actgccctgc aaaagctgga agaagctgaa aaagctgctg atgagagtga
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gagaggtatg aaggttattg aaaaccgggc cttaaaagat gaagaaaaga tggaactcca
                                                                     360
ggaaatccaa ctcaaagaag ctaagcacat tgcagaagag gcagatagga agtatgaaga
                                                                     420
ggtggctcgt aagttggtga tcattgaagg agacttggaa cgcacagagg aacgagctga
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gctggcagag tcccgttgcc gagagatgga tgagcagatt agactgatgg accagaacct
                                                                     540
gaagtgtctg agtgc
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ctcattccga tggacgaccg taatgcctac aggtgttttt cgcagccacg gcacatttct
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gttgcaatgg acaagttcgg gtttagcctg ccatatgttc agtattttgg aggtgtctct
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gctctcagta aacaacagtt tcttgccatc aatggattcc ctaataatta ttggggttgg
                                                                     300
ggaggagaag atgacgacat ttttaacaga ttagttcata aaggcatgtc tatatcacgt
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ccaaatgctg tagtagggag gtgtcgaatg atccggcatt caagagacaa gaaaaatgag
                                                                     420
cccaatcctc agaggtttga ccggatcgca catacaaagg aaacgatgcg cttcgatggt
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<210> 109
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                                                                     180
gatggtaaac aaacctgact gctatgagtt ttcaacccca tagtctaggg ccatgagggc
                                                                     240
gtcagttctt ggtggctgag ggtccttcca cccagcccac ctgggggagt ggagtgggga
                                                                     300
gttctgccag gtaagcagat gttgtctccc aagttcctga cccagatgtc tggcaggata
                                                                     360
acgctgacct gttccctcaa caagggacct gaaagtaatt ttgctcttta c
                                                                     411
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      <211> 451
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attatteeta gaaccaggeg acetgegaet eettgaegtt gacaategag tagtaeteee
                                                                     180
gattgaagcc cccattcgta taataattac atcacaagac gtcttgcact catgagctgt
                                                                     240
ccccacatta ggcttaaaaa cagatgcaat tcccggacgt ctaagccaaa ccactttcac
                                                                     300
cgctacacga ccgggggtat actacggtca atgctctgaa atctgtggag caaaccacag
                                                                     360
tttcatgccc atcgtcctag aattaattcc cctaaaaatc tttgaaatag ggdccgtatt
                                                                     420
taccctatag cacccctct accccctcta g
                                                                     451
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      <211> 541
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agaccaccac tgaccaggaa atgccacttt tacaaaatca tccccccttt tcatgattgg
                                                                     120
aacagttttc ctgaccgtct gggagcgttg aagggtgacc agcacatttg cacatgcaaa
                                                                    180
aaaggagtga ccccaaggcc tcaaccacac ttcccagagc tcaccatggg ctgcaggtga
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cttgccaggt ttggggttcg tgagctttcc ttgctgctgc ggtggggagg ccctcaagaa
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ctgagaggcc ggggtatgct tcatgagtgt taacatttac gggacaaaag cgcatcatta
                                                                    360
ggataaggaa cagccacagc acttcatgct tgtgagggtt agctgtagga gcgggtgaaa
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ggattccagt ttatgaaaat ttaaagcaaa caacggtttt tagctgggtg ggaaacagga
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aaactgtgat gtcggccaat gaccaccatt tttctgccca tgtgaaggtc cccatgaaac
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     <213> Homo sapien
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                                                                    120
cagtaccacc cctctctccc cactttccct ctcccggcaa catctctggg aatcaacagc
                                                                    180
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atattgacac gttggagccg agcctgaaca tgcccctcgg ccccagcaca tggaaaaccc
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tcatcagtcc attgctcttg agtctttgca gagaacctca gatcaggtgc acctgggaga
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aagactttgt ccccacttac agatctatct cctcccttgg gaagggcagg gaatggggac
                                                                       420
ggtgtatgga ggggaaggga tctcctgcgc ccttcattgc cacacttggt gggaccatga
                                                                       480
acatctttag tgtctgagct tctcaaatta ctgcaatagg a
                                                                       521
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      <213> Homo sapien
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agacattaaa gcaaaaatgc aagcaagtat agaaaaaggt ggttctcttc ccaaagtgga
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agccaaattc atcaattatg tgaagaattg cttccggatg actgaccaag aggctattca
                                                                       240
agatetetgg cagtggagga agtetettta agaaaatagt ttaaacaatt tgttaaaaaa
                                                                       300
ttttccgtct tatttcattt ctgtaacagt tgatatctgg ctgtcctttt tataatgcag
                                                                       360
agtgagaact ttccctaccg tgtttgataa atgttgtcca ggttctattg ccaagaatgt
                                                                       420
gttgtccaaa atgcctgttt agtttttaaa gatggaactc caccctttgc ttggttttaa
                                                                       480
gtatgtatgg aatgttatga taggacatag tagtagcggt ggtcagacat ggaaatggtg
                                                                       540
ggsmgacaaa aatatacatg tgaaataa
                                                                       568
      <210> 114
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tcggttttag taatctaggc tttgcctgta aagaatacaa cgatggattt taaatactgt
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ttgtggaatg tgtttaaagg attgattcta gaacctttgt atatttgata gtatttctaa
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ctttcatttc tttactgttt gcagttaatg ttcatgttct gctatgcaat cgtttatatg
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cacgtttctt taatttttt agattttcct ggatgtatag tttaaacaac aaaaagtcta
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tttaaaactg tagcagtagt ttacagttct agcaaagagg aaagttgtgg ggttaaactt
                                                                       360
tgtattttct ttcttataga ggcttctaaa aaggtatttt tatatqttct ttttaacaaa
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tattgtgtac aacctttaaa acatcaatgt ttggatcaaa acaagaccca gcttattttc
                                                                       480
tgc
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      <211> 521
      <212> DNA
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                                                                        60
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                                                                       120
gctgaatgaa attgtcggga atgaagacac cgtgagcagg ctagaggtct ttgcaaggga
                                                                       180
aggaaatgtg cccaacatca tcattgcggg ccctccagga accggcaaga ccacaagcat
                                                                       240
tetgtgettg geeegggeee tgetgggeee ageacteaaa qatqeeatqt tggaacteaa
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tgcttcaaat gacaggggca ttgacgttgt gaggaataaa attaaaatgt ttqctcaaca
                                                                       360
aaaagtcact cttcccaaag gccgacataa gatcatcatt ctggatgaag cagacagcat
                                                                       420
gaccgacgga gcccagcaag ccttgaggag aaccatggaa atctactcta aaaccactcg
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ttcgcccttg cttgtaatgc ttcggataag atcatcgagc c
                                                                       521
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      <211> 501
      <212> DNA
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agctgccttc cagcagcctg ccaaggccat ggcagagaga gactgcaaac aaacacaagc
                                                                        180
aaacagagtc tcttcacagc tggagtctga aagctcatag tggcatgtgt gaatctgaca
                                                                        240
aaattaaaag tgtgcatagt ccattacatg cataaaacac taataataat cctgtttaca
                                                                        300
cqtgactqca gcaggcaggt ccagctccac cactgccctc ctgccacatc acatcaagtg
                                                                        360
ccatggttta gagggttttt catatgtaat tcttttattc tgtaaaaggt aacaaaatat
                                                                        420
acagaacaaa actttccctt tttaaaaacta atgttacaaa tctgtattat cacttggata
                                                                        480
taaatagtat ataagctgat c
                                                                        501
      <210> 117
      <211> 451
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(451)
      <223> n = A, T, C or G
      <400> 117
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                                                                         60
ttagttctct ccctcccag cgtctccttc gtctccctgg ttttccgatg tccacagagt
                                                                       120
gagattgtcc ctaagtaact gcatgatcag agtgctgkct ttataagact cttcattcag
                                                                       180
cgtatccaat tcagcaattg cttcatcaaa tgccgttttt gccaggctac aggccttttc
                                                                       240
aggagagttt agaateteat agtaaaagae tgagaaattt agtgeeagae caagaegaat
                                                                       300
tgggtgtgta ggctgcattn ctttcttact aatttcaaat gcttcctggt aagcctgctg
                                                                       360
ggagttcgac acaagtggtt tgtttgttgc tccagatgcc acttcagaaa gatacctaaa
                                                                       420
ataatctcct ttcattttca aagtagaaca c
                                                                        451
      <210> 118
      <211> 501
      <212> DNA
      <213> Homo sapien
      <400> 118
teeggageeg gggtagtege egeegeegee geeggtgeag ceaetgeagg cacegetgee
                                                                        60
gccgcctgag tagtgggctt aggaaggaag aggtcatctc gctcggagct tcgctcggaa
                                                                       120
gggtctttgt tccctgcage cctcccacgg gaatgacaat ggataaaagt gagctggtac
                                                                       180
agaaagccaa actcgctgag caggctgagc gatatgatga tatggctgca gccatgaagg
                                                                       240
cagtcacaga acaggggcat gaactctcca acgaagagag aaatctgctc tctgttgcct
                                                                       300
acaagaatgt ggtaaggccg cccgccgctc ttcctggcgt gtcatctcca gcattgagca
                                                                       360
gaaaacagag aggaatgaga agaagcagca gatgggcaaa gagtaccgtg agaagataga
                                                                       420
ggcagaactg caggacatct gcaatgatgt tctggagctt gttggacaaa tatcttattc
                                                                       480
caatgctaca caacccagaa a
                                                                       501
      <210> 119
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<211> 391

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<212> DNA
      <213> Homo sapien
      <400> 119
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tgtgtgaggg gggaagcaac agcaaaagga agaaatgaga tgttgcaaaa aagatggagg
                                                                       120
agggttcccc tetectetgg ggactgacte aaacactgat gtggcagtat acaccattcc
                                                                       180
agagtcaggg gtgttcattc ttttttggga gtaagaaaag gtggggatta agaagacgtt
                                                                       240
tetggagget tagggaceaa ggetggtete ttteeceect eecaaceece ttgateeett
                                                                       300
tctctgatca ggggaaagga gctcgaatga gggaggtaga gttggaaagg gaaaggattc
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cacttgacag aatgggacag actccttccc a
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      <211> 421
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      <213> Homo sapien
      <220>
      <221> misc feature
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      <223> n = A, T, C or G
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                                                                       120
caccgagget gagageaaca tgaacgacet cgtetetgag tatcaagcag taccaggatg
                                                                       180
ccaccgcaga agaggaggag gatttcggtg aggaggccga agaggaggcc taaggcagag
                                                                       240
ccccatcac ctcaggcttc tcagttccct tagccgtctt actcaactgc ccctttcctc
                                                                       300
teceteagaa tttgtgtttg etgeetetat ettgtttttt gtttttett etgggggggt
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ctagaacagt gcctggcaca tagtaggcgc tcaataaata cttggttgnt gaatgtctcc
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t
                                                                       421
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      <211> 206
      <212> DNA
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      <400> 121
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aacccacgcc tgtaaggtcg gtcttcgtcc atctgctttt ttctgaaata cactaagagc
                                                                       120
agccacaaaa ctgtaacctc aaggaaacca taaagcttgg agtgccttaa tttttaacca
                                                                       180
gtttccaata aaacqqttta ctacct
                                                                       206
      <210> 122
      <211> 131
      <212> DNA
      <213> Homo sapien
      <400> 122
ggagatgaag atgaggaagc tgagtcagct acgggcargc gggcagctga agatgatgag
                                                                        60
gatgacgatg tcgataccaa gaagcagaag accgacgagg atgactagac agcaaaaaag
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gaaaagttaa a
                                                                       131
      <210> 123
      <211> 231
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<212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(231)
      <223> n = A, T, C or G
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cctcagtggc agtakgctaa kgaagatcaa gctacagsac atyatctaat atgaatgtta
                                                                       120
gcaattacat akcargaagc atgtttgctt tccagaagac tatggnacaa tggtcattwg
                                                                       180
ggcccaagag gatatttggc cnggaaagga tcaagataga tnaangtaaa q
                                                                       231
      <210> 124
      <211> 521
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(521)
      <223> n = A, T, C or G
      <400> 124
gagtagcaac gcaaagcgct tggtattgag tctgtgggsg acttcggttc cggtctctgc
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agcagccgtg atcgcttagt ggagtgctta gggtagttgg ccaggatgcc gaatatcaaa
                                                                       120
atcttcagca ggcagctccc accaggactt atctcasaaa attgctgacc gcctgggcct
                                                                       180
qqagctaggc aaggtggtga ctaagaaatt cagcaaccag gagacctgtg tggaaattgg
                                                                       240
tgaaagtgta ccgtggagag gatgtctaca ttgttcagag tggntgtggc gaaatcaatg
                                                                       300
acaatttaat ggagcttttg atcatgatta atgcctgcaa gattgcttca gccagccggg
                                                                       360
ttactgcagt catcccatgc ttcccttatg ccccggcagg ataagaaaga tnagagccgg
                                                                       420
gccgccaatc tcagccaagc ttggtgcaaa tatgctatct gtagcagtgc agatcatatt
                                                                       480
atcaccatgg acctacatgc ttctcaaatt canggctttt t
                                                                       521
      <210> 125
      <211> 341
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(341)
      <223> n = A, T, C or G
      <400> 125
atgcaaaagg ggacacaggg ggttcaaaaa taaaaatttc tcttcccct ccccaaacct
                                                                        60
gtaccccage teceegacca caacccctt ecteecegg ggaaagcaag aaggagcagg
                                                                       120
tgtggcatct gcagctggga agagagggc cggggaggtg ccgagctcgg tgctggtctc
                                                                       180
tttccaaata taaatacgtg tgtcagaact ggaaaatcct ccagcaccca ccacccaagc
                                                                       240
actotecgtt ttetgeeggt gtttggagag gggeggnggg eaggggegee aggeacegge
                                                                       300
tggctgcggt ctactgcatc cgctgggtgt gcaccccgcg a
                                                                       341
      <210> 126
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<211> 521

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<212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(521)
      <223> n = A, T, C or G
      <400> 126
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caggeceaga gtggcactgg acagaceatg caggtgatge ageagateat cactaacaca
                                                                       120
ggagagatec ageagatece ggtgeagetg aatgeeggee agetgeagta tateegetta
                                                                       180
gcccagcctg tatcaggcac tcaagttgtg cagggacaga tccagacact tgccaccaat
                                                                       240
gctcaacaga ttacacagac agaggtccag caaggacagc agcagttcaa gccagttcac
                                                                       300
aagatggaca gcagctctac cagatccagc aagtcaccat gcctqcqqqc canqacctcq
                                                                       360
ccagcccatg ttcatccagt caagccaacc agcccttcna cgggcaggcc ccccaggtqa
                                                                       420
ccggcgactg aagggcctga gctggcaagg ccaangacac ccaacacaat ttttgccata
                                                                       480
cagococcag gcaatgggca cagootttot toccagagga c
                                                                       521
      <210> 127
      <211> 351
      <212> DNA
      <213> Homo sapien
      <400> 127
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aatgcattta aaaaataaaa gggaggtggg cagcaaacac acaaagtcct agtttcctgg
                                                                       120
gtccctggga gaaaagagtg tggcaatgaa tccacccact ctccacaggg aataaatctg
                                                                       180
tctcttaaat gcaaagaatg tttccatggc ctctggatgc aaatacacag agctctgggg
                                                                       240
tcaqaqcaaq qqatqqqqaq aqqaccacqa qtqaaaaaqc aqctacacac attcacctaa
                                                                       300
ttccatctqa qqqcaaqaac aacqtqqcaa qtcttqqqqq taqcaqctqt t
                                                                       351
      <210> 128
      <211> 521
      <212> DNA
      <213> Homo sapien
      <400> 128
tocagacatg ctcctgtcct aggcggggag caggaaccag acctgctatg ggaagcagaa
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agagttaagg gaaggtttcc tttcattcct gttccttctc ttttgctttt gaacagtttt
                                                                       120
taaatatact aatagctaag tcatttgcca gccaggtccc ggtgaacagt agagaacaag
                                                                       180
gagettgeta agaattaatt ttgetgtttt teaccecatt caaacagage tgeeetgtte
                                                                       240
cctgatggag ttccattcct gccagggcac ggctgagtaa cacgaagcca ttcaagaaag
                                                                       300
gegggtgtga aatcactgcc accccatgga cagacccctc actcttcctt cttagccgca
                                                                       360
gcgctactta ataaatatat ttatactttg aaattatgat aaccgatttt tcccatgcgg
                                                                       420
catcctaagg gcacttgcca gctcttatcc ggacagtcaa gcactgttgt tggacaacag
                                                                       480
ataaaggaaa agaaaaagaa gaaaacaacc gcaacttctg t
                                                                       521
      <210> 129
      <211> 521
      <212> DNA
      <213> Homo sapien
      <400> 129
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cagatctagt ggcagagagg aagatgatga ggaacttctg agacgtcggc agcttcaaga
                                                                       120
agagcaatta atgaagctta actcaggcct gggacagttg atcttgaaag aagagatgga
                                                                       180
qaaaqagagc cgggaaaggt catctctgtt agccagtcgc tacgattctc ccatcaactc
                                                                       240
agetteacat attecateat etaaaaetge ateteteet ggetatggaa gaaatggget
                                                                       300
tcaccggcct gtttctaccg acttcgctca gtataacagc tatggggatg tcagcggggg
                                                                       360
agtgcgagat taccagacac ttccagatgg ccacatgcct gcaatgagaa tggaccgagg
                                                                       420
aqtqtctatg cccaacatgt tggaaccaaa gatatttcca tatgaaatgc tcatggtgac
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caacagaggg ccgaaaccaa atctcagaga ggtggacaga a
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      <211> 270
      <212> DNA
      <213> Homo sapien
      <400> 130
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ctgcacggag actctggtgt gggtcttgac gaggtggtca gtgaactcct gatagggaga
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cttggtgaat acagtctcct tccagaggtc gggggtcagg tagctgtagg tcttagaaat
                                                                       180
ggcatcaaag gtggccttgg cgaagttgcc cagggtggca gtgcagcccc gggctgaggt
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gtagcagtca tcgataccag ccatcatgag
                                                                       270
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      <211> 341
      <212> DNA
      <213> Homo sapien
      <400> 131
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ccaqccattc gctcctactg atgagacaag atgtggtgat gacagaatca gcttttgtaa
                                                                       120
ttatgtataa tagctcatgc atgtgtccat gtcataactg tcttcatacg cttctgcact
                                                                       180
ctqqqqaaga aggagtacat tgaagggaga ttggcaccta gtggctggga gcttgccagg
                                                                       240
aacccagtgg ccagggagcg tggcacttac ctttgtccct tgcttcattc ttgtqaqatq
                                                                       300
ataaaactgg gcacagctct taaataaaat ataaatgaac a
                                                                       341
      <210> 132
      <211> 844
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature...
      <222> (1)...(844)
      <223> n = A, T, C or G
      <400> 132
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gaaccttcca gaagtgggca tctgtggtgg tgcctcttgg gaaggagcag aagtacacat
                                                                       120
gccatgtgga acatgagggg ctgcctgagc ccctcaccct gagatggggc aaggaggagc
                                                                       180
etecticate caccaagact aacacagtaa teatigetgi teeggitgie etiggagetg
                                                                       240
tggtcatcct tggagctgtg atggcttttg tgatgaagag gaggagaaac acaggtggaa
                                                                       300
aaggagggga ctatgctctg gctccaggct cccagagctc tgatatgtct ctcccagatt
                                                                       360
gtaaagtgtg aagacagctg cctggtgtgg acttggtgac agacaatgtc ttcacacatc
                                                                       420
tectgtgaca tecagagace teagttetet ttagteaagt gtetgatgtt eeetgtgagt
                                                                       480
ctgcgggctc aaagtgaaga actgtggagc ccagtccacc cctgcacacc aggaccctat
                                                                       540
contgeactg contgtgtto cottonacag coaaccttge tgctonaged aaacattggt
                                                                       600
```

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ggacatctgc agcetgtcag ctccatgcta ccctgacctt caactcctca cttccacact
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gagaataata atttgaatgt gggtggctgg agagatggct cagcgctgac tgctcttcca
                                                                       720
aaggteetga gtteaaatee eageaaceae atggtggete acaaceatet gtaatgggat
                                                                       780
ctaataccct cttctgcagt gtctgaagac asctacagtg tacttacata taataataaa
                                                                       840
taag
                                                                       844
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      <211> 601
      <212> DNA
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      <400> 133
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agcaagcagc gagtettgaa getetgtttg gtgetttgga tecattteca teggteetta
                                                                       120
cageegeteg teagaeteea geageeaaga tggtgaagea gategagage aagaetgett
                                                                       180
ttcaqgaagc cttggacgct gcaggtgata aacttgtagt agttgacttc tcagccacgt
                                                                       240
ggtgtgggcc ttgcaaaatg atcaagcctt tctttcattc cctctctgaa aagtattcca
                                                                       300
acgtgatatt ccttgaagta gatgtggatg actgtcagga tgttgcttca gagtgtgaag
                                                                       360
tcaaatgcat gccaacattc cagtttttta agaagggaca aaaggtgggt gaattttctg
                                                                       420
gagccaataa ggaaaagctt gaagccacca ttaatgaatt agtctaatca tgttttctga
                                                                       480
aaatataacc agccattggc tatttaaaac ttgtaatttt tttaatttac aaaaatataa
                                                                       540
aatatgaaga cataaacccm gttgccatct gcgtgacaat aaaacattaa tgctaacact
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      <212> DNA
      <213> Homo sapien
      <400> 134
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agagaaaccc ttccctccct ccacctccct ccccaccct cctcatgaat taagaatcta
                                                                       120
agagaagaag taaccataaa accaagtttt gtggaatcca tcatccagag tgcttacatg
                                                                       180
gtgattaggt taatattgcc ttcttacaaa atttctattt taaaaaaaat tataaccttg
                                                                       240
attgcttatt acaaaaaat tcagtacaaa agttcaatat attgaaaaat gcttttcccc
                                                                       300
teceteacag cacegittia tatatageag agaataatga agagatiget agictagatg
                                                                       360
gggcaatett caaattacae caagaegeae agtggtttat ttacceteee etteteataa
                                                                       420
                                                                       421
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      <211> 511
      <212> DNA
      <213> Homo sapien
      <400> 135
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gctgacagac aaagagagag agatggcgga aataagggat caaatgcagc aacagctgaa
                                                                       120
tgactatgaa cagcttcttg atgtaaagtt agccctggac atggaaatca gtgcttacag
                                                                       180
gaaactctta gaaggcgaag aagagaggtt gaagctgtct ccaagccctt cttcccgtgt
                                                                       240
gacagtatee egageateet caagtegtag tgtacegtae aactagagga aageggaaga
                                                                       300
gggttgatgt ggaagaatca gaggcgaagt agtagtgtta gcatctctca ttccgcctca
                                                                       360
accactggaa atgtttgcat cgaagaaatt gatgttgatg ggaaatttat cccgcttgaa
                                                                       420
gaacacttct gaacaggatc aaccaatggg aaggcttggg agatgatcag aaaaattgga
                                                                       480
gacacatcag tcagttataa atatacctca a
                                                                       511
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<210> 136
      <211> 341
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      <213> Homo sapien
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gcctcggcct cccaaagtgc tgggattaca ggcgtgagcc accacgcccg gcccccaaag
                                                                     120
ctgtttcttt tgtctttagc gtaaagctct cctgccatgc agtatctaca taactgacgt
                                                                     180
gactgccage aagetcagte acteegtggt etttteetet ttecagttet tetetete
                                                                     240
ttcaagttct gcctcagtga aagctgcagg tccccagtta agtgatcagg tgagggttct
                                                                     300
ttgaacctgg ttctatcagt cgaattaatc cttcatgatg g
                                                                     341
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      <400> 137
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                                                                     120
aattattgtg tcagaagaga ttgaatacct gcttaagaag cttacagaag ctatgggagg
                                                                     180
aggttggcag caagaacaat ttgaacatta taaaatcaac tttgatgaca gtaaaaatgg
                                                                     240
cctttctgca tgggaactta ttgagcttat tggaaatgga cagtttagca aaggcatgga
                                                                     300
ccggcagact gtgtctatgg caattaatga agtctttaat gaacttatat tagatgtgtt
                                                                     360
aaaqcagggt tacatgatga aaaagggcca cagacggaaa aactggactg aaagatggtt
                                                                     420
tgtactaaaa cccaacataa tttcttacta tgtgagtgag gatctgaagg ataagaaagg
                                                                     480
agacattctc ttggatgaaa attgctgtgt agaagtcctt gcctgacaaa agatggaaag
                                                                     540
aaatgccttt t
                                                                     551
      <210> 138
     <211> 531
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc feature
     <222> (1)...(531)
     <223> n = A, T, C or G
     <400> 138
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ttgatttctc tttctcccaa tcggccccaa agagaccaca taaaaggaga gtacatttta
                                                                     120
agccaataag ctgcaggatg tacacctaac agacctccta gaaaccttac cagaaaatgg
                                                                     180
ggactgggta gggaaggaaa cttaaaaagat caacaaactg ccagcccacg gactgcagag
                                                                     240
300
atataaaaatt taaaaagttt tgtacataag ctattcaaga tttctccagc actgactgat
                                                                     360
acaaagcaca attgagatgg cacttctaga gacagcagct tcaaacccag aaaagggtga
                                                                     420
tgagatgaag tttcacatgg ctaaatcagt ggcaaaaaca cagtcttctt tctttctttc
                                                                     480
tttcaaggan gcaggaaagc aattaagtgg tcaccttaac ataaggggga c
                                                                     531
     <210> 139
     <211> 521
     <212> DNA
     <213> Homo sapien
                                                    E . . .
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<220>
      <221> misc feature
      <222> (1)...(521)
      <223> n = A, T, C or G
      <400> 139
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ctgcagcagc aggcagatga tgcagaggag cgagctgaqc qcctccaqcq agaaqttgaq
                                                                       120
ggagaaaggc gggcccggga acaggctgag gctgaggtgg cctccttgaa ccgtaggatc
                                                                       180
cagctggttg aagaagagct ggaccgtgct caggagcgcc tggccactgc cctgcaaaag
                                                                       240
ctggaagaag ctgaaaaagc tgctgatgag agtgagagag gtatgaaggt tattgaaaac
                                                                       300
cgggccttaa aagatgaaga aaagatggaa ctccaggaaa tccaactcaa aqaagctaaq
                                                                       360
cacattgcag aagaggcaga taggaagtat gaagaggtgg ctcgtaagtt ggtgatcatt
                                                                       420
qaaqqagact tggaaccgca cagaaggaac gagcttgagc ttggcaaaag tcccgttgcc
                                                                       480
cagagatggg atgaaccaga ttagactgat ggaccanaac c
                                                                       521
      <210> 140
      <211> 571
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(571)
      <223> n = A, T, C \text{ or } G
      <400> 140
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ctggaagcgc cccgagagtg acagcgtgag gctgggaggg aggacttggc ttgagcttgt
                                                                       120
taaactctgc tctgagcctc cttgtcgcct qcatttaqat gqctcccqca aaqaaqqqtq
                                                                        180
gcgagaagaa aaagggccgt tctgccatca acgaaqtqqt aacccqaqaa tacaccatca
                                                                        240
acattcacaa gegeateeat ggagtggget teaagaageg tgeacetegg geacteaaag
                                                                       300
agattcggaa atttgccatg aaggagatgg gaactccaga tgtgcgcatt gacaccaggc
                                                                        360
tcaacaaaqc tqtctqqqcc aaaqqaataa qqaatqtqcc ataccqaatc cqqtqtqcqq
                                                                        420
ctgtccagaa aacgtaatga ggatgaagat tcaccaaata agctatatac tttggttacc
                                                                        480
tatgtacctg ttaccacttt caaaaatcta cagacagtca atgtggatga gaactaatcg
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                                                                        571
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      <211> 531
      <212> DNA
      <213> Homo sapien
      <400> 141
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                                                                         60
aatggggagg cetettggag acacagaggg ttteacettg gatgacetet agagaaattg
                                                                        120
eccaagaage ecacettetg gteccaacet geagaceeca eageagteag ttggteagge
                                                                        180
cctgctgtag aaggtcactt ggctccattg cctgcttcca accaatgggc aggagagaag
                                                                        240
gootttattt ctcgcccacc cattcctcct gtaccagcac ctccqttttc agtcagtqtt
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gtccagcaac ggtaccgttt acacagtcac ctcagacaca ccatttcacc tcccttqcca
                                                                        360
agctgttagc cttagagtga ttgcagtgaa cactgtttac acaccgtgaa tccattccca
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tcagtccatt ccagttggca ccagcctgaa ccatttggta cctggtgtta actggagtcc
                                                                        480
tgtttacaag gtggagtcgg ggcttgctga cttctcttca tttgagggca c
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```

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<210> 142
      <211> 491
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(491)
      <223> n = A, T, C or G
      <400> 142
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51

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ategeegtee acattgetea cagggactgg gaaggegatg cetgteggga getgetggtg
                                                                       300
gagagacteg ggatgactee tgeteagatt caggeettge teaggaaagg ggaaaagttt
                                                                       360
ggtcgaggag tgatagcggg actcgttgac attggggaaa ctttgcaatg ccccgaagac
                                                                       420
ttaactcccg atgaggttgt ggaactagaa aatcaagctg cactgaccaa cctgaagcag
                                                                       4.80
aagtacctga ctgtgatttc aaaccccagg tggttactgg agcccatacc taggaaagga
                                                                       540
ggcaaggatg tattccaggt agacatccca gagcacctga tccctttggg gcatgaagtg
                                                                       600
tgacaagtgt gggctcctga aaggaatgtt ccrgaqaaac caqctaaatc atqqcacctt
                                                                       660
caatttgcca tcgtgacgca gacctgtata aattaggtta aagatgaatt tccactgctt
                                                                       720
tggagagtcc cacccactaa gcactgtgca tgtaaacagg ttcctttgct cagatgaagg
                                                                       780
aagtaggggg tggggctttc cttgtgtgat gcctccttag gcacacaggc aatqtctcaa
                                                                       840
gtactttgac cttagggtag aaggcaaagc tgccagtaaa tgtctcagca ttgctgctaa
                                                                       900
ttttggtcct gctagtttct ggattgtaca aataaatqtq ttgtagatqa
                                                                       950
      <210> 163
      <211> 475
      <212> DNA.
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(475)
     <223> n = A, T, C or G
     <400> 163
tegageggee geeegggeag gtgteggagt ceageaeggg aggegtggte ttgtagttqt
                                                                        60
totocggotg cocattgoto toccactoca eggogatgto gotgggatag aagootttga
                                                                       120
ccaggcaggt caggctgace tggttettgg teateteete eegggatggg ggeagggtgt
                                                                       180
acacctgtgg ttctcggggc tgccctttgg ctttggagat ggttttctcg atgggggctg
                                                                       240
ggagggettt gttggagace ttgeacttgt acteettgee atteaaceag teetggtgea
                                                                       300
```

```
ngacggtgag gacgctnacc acacggtacg ngctggtgta ctgctcctcc.cgcggctttg
                                                                       360
tettggcatt atgeaectee aegeegteea egtaceaatt gaaettgaee teagggtett
                                                                       420
cgtggctcac gtccaccacc acgcatgtaa cctcaaanct cggncgcgan cacgc
                                                                       475
      <210> 164
      <211> 476
      <212> DNA
      <213> Homo sapien
      <400> 164
agcgtggtcg cggccgaggt ctgaggttac atgcgtggtg gtggacgtga gccacgaaga
                                                                        60
ccctgaggtc aagttcaact ggtacgtgga cggcgtggag gtgcataatg ccaagacaaa
                                                                       120
gccgcgggag gagcagtaca acagcacgta ccgtgtggtc agcgtcctca ccgtcctgca
                                                                       180
ccaggactgg ctgaatggca aggagtacaa gtgcaaggtc tccaacaaag ccctcccagc
                                                                       240
ccccatcgag aaaaccatct ccaaagccaa agggcagccc cgagaaccac aggtgtacac
                                                                       300
cctqccccca tcccgggagg agatgaccaa gaaccaggtc agcctgacct gcctggtcaa
                                                                       360
aggettetat eccagegaca tegecegtgg agtgggagag caatgggeag eeggagaaca
                                                                       420
actacaagac cacgeeteee gtgetggaet cegacacetg eegggeggee getega
                                                                       476
      <210> 165
      <211> 256
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(256)
      <223> n = A, T, C or G
      <400> 165
agcgtggttn cggccgaggt cccaaccaag gctgcancct ggatgccatc aaagtcttct
                                                                        60
gcaacatgga gactggtgag acctgcgtgt accccactca gcccagtgtg gcccagaaga
                                                                       120
actggtacat cagcaagaac cccaaggaca agaggcatgt ctggttcggc gagagcatga
                                                                       180
ccgatggatt ccagttcgag tatggcggcc agggctccga ccctgccgat gtggacctgc
                                                                       240
ccgggcggnc gctcga
                                                                       256
      <210> 166
      <211> 332
      <212> DNA
      <213> Homo sapien
   .. <400> 166
agcgtgdtcg cggccgaggt caagaacccc gccgcacct gccgtgacct caagatgtgc
                                                                        60
cactctgact ggaagagtgg agagtactgg attgacccca accaaggctg caacctggat
                                                                       120
gccatcaaag tettetgcaa catggagaet ggtgagaeet gegtgtaeee caeteageee
                                                                       180
agtgtggccc agaagaactg gtacatcagc aagaacccca aggacaagag gcatgtctgg
                                                                       240
ttcggcgaga gcatgaccga tggattccag ttcgagtatg gcggccaggg ctccgaccet
                                                                       300
gccgatgtgg acctgcccgg gcggccgctc ga
                                                                       332
      <210> 167
      <211> 332
      <212> DNA
     <213> Homo sapien
     <220>
```

```
<221> misc feature
      <222> (1)...(332)
      <223> n = A, T, C or G
      <400> 167
tegageggte gecegggeag gtecaeateg geagggtegg agecetggee gecatacteg
                                                                         60
aactggaatc catcggncat gctctcgccg aaccagacat gcctcttgnc cttggggttc
                                                                        120
ttqctgatgt accagntctt ctgggccaca ctgggctgag tggggtacac gcaggtctca
                                                                        180
ccantctcca tgttgcanaa gactttgatg gcatccaggt tgcagccttg gttggggtca
                                                                        240
atccagtact ctccactctt ccagacagag tggcacatct tgaggtcacg gcaggtgcgg
                                                                        300
gcggggttct tgacctcggt cgcgaccacg ct
                                                                        332
      <210> 168
      <211> 276
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(276)
      <223> n = A, T, C or G
      <400> 168
tcgagcggcc gcccgggcag gtcctcctca gagcggtagc tgttcttatt gccccggcag
                                                                        60
cctccataga tnaagttatt geangagtte ctctccacgt caaagtacca gcgtgggaag
                                                                       120
gatgcacggc aaggcccagt gactgcgttg gcggtgcagt attcttcata gttgaacata
                                                                       180
tegetggagt ggaetteaga ateetgeett etgggageae ttgggacaga ggaateeget
                                                                       240
gcattcctgc tggtggacct cggccgcgac cacqct
                                                                       276
      <210> 169
      <211> 276
      <212> DNA
      <213> Homo sapien
      <400> 169
agegtggteg eggeegaggt ceaceageag gaatgeageg gatteetetg teceaagtge
                                                                        60
teceagaagg caggattetg aagaceaete cagegatatg tteaactatg aagaataetg
                                                                       120
caccgccaac gcagtcactg ggccttgccg tgcatccttc ccacgctgqt actttgacgt
                                                                       180
ggagaggaac tcctgcaata acttcatcta tggaggctgc cggggcaata agaacagcta
                                                                       240
ccgctctgag gaggacctgc ccgggcggcc gctcga
                                                                       276
      <210> 170
      <211> 332
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(332)
      <223> n = A, T, C or G
      <400> 170
tegageggee geeeggeag gtecaeateg geagggtegg agecetggee geeatacteg
                                                                        60
aactggaatc catcggtcat gctctcgccg aaccagacat gcctcttgtc cttggggttc
                                                                       120
ttgctgatgt accagttctt ctgggccaca ctgggctgag tggggtacac gcaggtctca
                                                                       180
```

3 1

```
ccagteteca tgttgcagaa gactttgatg gcatecaggt tgcageettq qttqqqqtea
                                                                       240
atccagtact ctccactett ccagccagaa tggcacatet tgaggtcacg qcangtgegg
                                                                       300
geggggttet tgacetegge egegaceaeg et
                                                                       332
      <210> 171
      <211> 333
      <212> DNA
      <213> Homo sapien
      <400> 171
agogtggtog cggccgaggt caagaaaccc cgcccgcacc tgccgtgacc tcaagatgtg
                                                                        60
ccactctggc tggaagagtg gagagtactg gattgacccc aaccaaggct gcaacctqqa
                                                                       120
tgccatcaaa gtcttctgca acatggagac tggtgagacc tgcgtgtacc ccactcagcc
                                                                       180
cagtgtggcc cagaagaact ggtacatcag caagaacccc aaggacaaga ggcatgtctg
                                                                       240
qctcqgcgag agcatgaccg atggattcca gttcgagtat ggcggccagg gctccgaccc
                                                                       300
tgccgatgtg gacctgcccg ggcggccgct cga
                                                                       333
      <210> 172
      <211> 527
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(527)
      <223> n = A, T, C or G
      <400> 172
agcgtggtcg cggccgaggt cctgtcagag tggcactggt agaagntcca ggaaccctga
                                                                        60
actgtaaggg ttcttcatca gtgccaacag gatgacatga aatgatgtac tcagaagtgt
                                                                       120
cctgnaatgg ggcccatgan atggttgnct gagagagagc ttcttgtcct acattcggcg
                                                                       180
ggtatggtct tggcctatgc cttatggggg tggccgttgn gggcggtgng gtccgcctaa
                                                                       240
aaccatgttc ctcaaagatc atttgttgcc caacactggg ttgctgacca naagtgccag
                                                                       300
gaagctgaat accatttcca gtgtcatacc cagggtgggt gacgaaaggg gtcttttgaa
                                                                       360
ctgtggaagg aacatccaag atctctgntc catgaagatt ggggtgtgga agggttacca
                                                                       420
gttggggaag ctcgctgtct ttttccttcc aatcangggc tcgctcttct gaatattctt
                                                                       480
cagggcaatg acataaattg tatattcggt tcccggttcc aggccag
                                                                       527
      <210> 173
      <211> 635
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(635)
      <223> n = A, T, C or G
      <400> 173
togagoggeo geoogggoag gtocaccaca cocaattect tgctggtate atggcageog
                                                                        60
ccacgtgcca ggattaccgg ctacatcatc aagtatgaga agcctgggtc tcctcccaga
                                                                       120
gaagtqqtcc ctcqqccccg ccctggtqtc acaqaqqcta ctattactqq cctqqaaccq
                                                                       180
ggaaccgaat atacaattta tgtcattgcc ctgaagaata atcagaagag cgagccctg
                                                                       240
attggaagga aaaagacaga cgagetteee caactggtaa eeetteeaca eeecaatett
                                                                       300
catggaccag agatettgga tgtteettee acagtteaaa agacceettt egteaceeae
                                                                       360
```

```
cctgggtatg acactggaaa tggtattcag cttcctggca cttctggtca gcaacccagt
                                                                        420
gttgggcaac aaatgatctt tgangaacat ggntttaggc ggaccacacc ggccacaacg
                                                                        480
qqcaccccca taaggcatag gccaagaaca tacccgncga atgtaggaca agaagctctn
                                                                        540
totcanacaa neatoteatg ggeoceatte cangacaett etgagtaeat cantteatgg
                                                                        600
catcctggtg gcactgataa aaacccttac agtta
                                                                        635
      <210> 174
      <211> 572
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(572)
      <223> n = A, T, C or G
      <400> 174
agcgtggtcg cgggcgaggt cctgtcagag tggcactggt agaagttcca ggaaccctga
                                                                         60
actgtaaggg ttcttcatca gtgccaacag gatgacatga aatgatgtac tcagaagtgt
                                                                        120
cctggaatgg ggcccatgag atggttgtct gagagagagc ttcttgtcct acattcggcg
                                                                        180
ggtatggtct tggcctatgc cttatggggg tggccgttgt gggcggtgtg gtccgcctaa
                                                                        240
aaccatgttc ctcaaagatc atttgttgcc caacactggg ttgctgacca gaagtgccag
                                                                        300
gaagctgaat accatttcca gtgtcatacc cagggtgggt gacgaaaggg gtcttttgaa
                                                                        360
ctgtggaagg aacatccaag atctctggtc catgaagatt ggggtgtgga agggttacca
                                                                        420
gttggggaag ctcgtctgtc tttttccttc caatcanggg ctcgctcttc tgattattct
                                                                        480
tcagggcaat gacataaatt gtatattcgg ntcccgggtn cagccaataa taataaccct
                                                                       540
ctgtgacacc anggcggggc cgaagganca ct
                                                                       572
      <210> 175
      <211> 372
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(372)
      <223> n = A, T, C or G
      <400> 175
agcgtggtcg cggccgaggt cctcaccaga ggtaccacct acaacatcat agtggaggca
                                                                        60
ctgaaagacc agcagaggca taaggttcgg gaagaggttg ttaccgtggg caactctgtc
                                                                       120
aacgaaggct tgaaccaacc tacggatgac tcgtgctttg acccctacac agtttcccat
                                                                       180
tatgccgttg gagatgagtg ggaacgaatg tctgaatcag gctttaaact gttgtgccag
                                                                       240
tgcttangct ttggaagtgg tcatttcaga tgtgattcat ctagatggtg ccatgacaat
                                                                       300
ggtgtgaact acaagattgg agagaagtgg gaccgtcagg gagaaaatgg acctgcccgg
                                                                       360
geggeegete ga
                                                                       372
      <210> 176
      <211> 372
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(372)
```

```
<223> n = A, T, C or G
      <400> 176
tegageggee geeegggeag gteeatttte teeetgaegg teeeacttet etecaatett
                                                                         60
gtagttcaca ccattgtcat ggcaccatct agatgaatca catctgaaat gaccacttcc
                                                                        120
aaagcctaag cactggcaca acagtttaaa gcctgattca gacattcgtt cccactcatc
                                                                        180
tccaacggca taatgggaaa ctgtgtaggg gtcaaagcac gagtcatccg taggttggtt
                                                                        240
caageetteg ntgacagagt tgeecaeggt aacaacetet teeegaacet tatgeetetg
                                                                        300
ctggtctttc agtgcctcca ctatgatgtt gtaggtggta cctctggtga ggacctcggc
                                                                        360
cgcgaccacg ct
                                                                        372
      <210> 177
      <211> 269
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(269)
      <223> n = A, T, C or G
      <400> 177
agegtggeeg eggeegaggt ceattggetg gaacggeate aacttggaag ceagtgateg
                                                                         60
teteageett ggtteteeag etaatggtga tggnggtete agtageatet gteacaegag
                                                                        120
cccttcttgg tgggctgaca ttctccagag tggtgacaac accctgagct ggtctgcttg
                                                                        180
tcaaagtgtc cttaagagca tagacactca cttcatattt ggcgnccacc ataagtcctg
                                                                        240
atacaaccac ggaatgacct gtcaggaac
                                                                        269
      <210> 178
      <211> 529
      <212> DNA
      <213> Homo sapien
      <400> 178
tegageggee geeegggeag gteeteagae egggttetga gtacacagte agtgtggttg
                                                                         60
cettgeacga tgatatggag agceageece tgattggaac ceagteeaca getatteetg
                                                                        120
caccaactga cctgaagttc actcaggtca cacccacaag cctgagcgcc cagtggacac
                                                                        180
cacccaatgt tcagctcact ggatatcgag tgcgggtgac ccccaaggag aagaccggac
                                                                        240
caatgaaaga aatcaacctt gctcctgaca gctcatccgt ggttgtatca ggacttatgg
                                                                        300
cggccaccaa atatgaagtg agtgtctatg ctcttaagga cactttgaca agcagaccag
                                                                        360
ctcagggtgt tgtcaccact ctggagaatg tcagcccacc aagaagggct cgtgtgacag
                                                                        420
atgctactga gaccaccatc accattagct ggagaaccaa gactgagacg atcactggct
                                                                        480
tccaagttga tgccgttcca gccaatggac ctcggccgcg accacgctt
                                                                        529
      <210> 179
      <211> 454
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(454)
      \langle 223 \rangle n = A, T, C or G
      <400> 179
```

```
agcgtggtcg cggccgaggt ctggccgaac tgccagtgta cagggaagat gtacatgtta
                                                                          60
tagntettet egaagteeeg ggeeageage teeaeggggt ggteteetge eteeaggege
                                                                         120
ttctcattct catggatctt cttcacccgc agcttctgct tctcagtcag aaggttgttg
                                                                         180
tecteatece teteatacag ggtgaccagg aegttettga gecagteceg catgegeagg
                                                                         240
gggaattcgg tcagctcaga gtccaggcaa ggggggatgt atttgcaagg cccgatgtag
                                                                         300
tccaagtgga gcttgtggcc cttcttggtg ccctccaagg tgcactttgt ggcaaagaag
                                                                         360
tggcaggaag agtcgaaggt cttgttgtca ttgctgcaca ccttctcaaa ctcgccaatg
                                                                         420
ggggctgggc agacctgccc gggcggccgc tcga
                                                                         454
      <210> 180
      <211> 454
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(454)
      <223> n = A, T, C or G
      <400> 180
tcgagcggcc gcccgggcag gtctgcccag ccccattgg cgagtttgag aaggngtgca
                                                                         60
gcaatgacaa caagacette gactetteet gecaettett tgccacaaag tgcaeeetgg
                                                                        120
agggcaccaa gaagggccac aagctccacc tggactacat cgggccttgc aaatacatcc
                                                                        180
ccccttgcct ggactctgag ctgaccgaat tccccctgcg catgcgggac tggctcaaga
                                                                        240
acgtcctggt caccctgtat gagagggatg aggacaacaa ccttctgact qagaagcana
                                                                        300.
agctgcgggt gaagaanatc catgagaatg anaagcgcct gnaggcanga gaccaccccg
                                                                        360
tggagctgct ggcccgggac ttcgagaaga actataacat qtacatcttc cctqtacact
                                                                        420
ggcagttcgg ccagacctcg gccgcgacca cgct
                                                                        454
      <210> 181
      <211> 102
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(102)
      <223> n = A, T, C \text{ or } G
      <400> 181
agcgtggntg cggacgacgc ccacaaagcc attgtatgta gttttanttc agctgcaaan
                                                                         60
aataccncca gcatccacct tactaaccag catatgcaga ca
                                                                        102 _
      <210> 182
      <211> 337
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(337)
      \langle 223 \rangle n = A, T, C or G
      <400> 182
tcgagcggtc gcccgggcag gtctgggcgg atagcaccgg gcatattttg gaatggatga
                                                                         60
```

```
ggtctggcac cctgagcagc ccagcgagga cttggtctta gttgagcaat ttggctagga
                                                                         120
 ggatagtatg cagcacggtt ctgagtctgt gggatagctg ccatgaagna acctgaagga
                                                                         180
 ggcgctggct ggtangggtt gattacaggg ctgggaacag ctcgtacact tgccattctc
                                                                         240
 tgcatatact ggntagtgag gcgagcctgg cgctcttctt tgcgctgagc taaagctaca
                                                                         300
 tacaatqqct ttqnqgacct cggccgcqac cacqctt
                                                                         337
        <210> 183
        <211> 374
        <212> DNA
        <213> Homo sapien
        <400> 183
 tegageggee gecegggeag gtecatttte teeetgaegg teceaettet etecaatett
                                                                          60
 qtaqttcaca ccattgtcat gacaccatct agatgaatca catctgaaat gaccacttcc
                                                                         120
 aaaqcctaag cactggcaca acagtttaaa gcctgattca gacattcgtt cccactcatc
                                                                         180
 tecaaeggea taatgggaaa etgtgtaggg gteaaageae gagteateeg taggttggtt
                                                                         240
 caageetteg ttgacagaag ttgcccacgg taacaacete ttcccgaace ttatgcctet
                                                                         300
 gctggtcttt caagtgcctc cactatgatg ttgtaggtgg cacctctggt gaggacctcg
                                                                         360
- geogegacea eget
                                                                         374
        <210> 184
        <211> 375
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(375)
        <223> n = A, T, C or G
        <400> 184
                                                                          60
  aqcqtqqttt gcggccgagg tcctcaccan aggtgccacc tacaacatca tagtggaggc
                                                                         120
  actgaaagac cagcagaggc ataaggttcg ggaagaggtt gttaccgtgg gcaactctgt
  caacqaaggc ttgaaccaac ctacggatga ctcgtgcttt gacccctaca cagnttccca
                                                                         180
  ttatqccqtt ggagatgagt gggaacgaat gtctgaatca ggctttaaac tgttgtgcca
                                                                         240
  qtqcttanqc tttggaagtg gtcatttcag atgtgattca tctanatggt gtcatgacaa
                                                                         300
  tggtgngaac tacaagattg gagagaagtg gnaccgtcag ggganaaaat ggacctgccc
                                                                         360
  gggcggcncg ctcga
                                                                         375
        <210> 185
        <211> 148
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc feature
        <222> (1)...(148)
        <223> n = A, T, C or G
        <400> 185
  ageqtggteg eggeegaggt etggettnet geteangtga ttateetgaa eeateeagge
                                                                          60
  caaataagcg ccggctatgc ccctgnattg gattgccaca cggctcacat tgcatgcaag
                                                                         120
  tttgctgagc tgaaggaaaa gattgatc
                                                                         148
```

<210> 186

```
<211> 397
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(397)
      <223> n = A, T, C or G
      <400> 186
tegageggee geeegggeag gteeaattga aacaaacagt tetgagaeeg ttetteeace
                                                                         60
actgattaag agtggggngg cgggtattag ggataatatt catttagcct tctgagcttt
                                                                        120
ctgggcagac ttggtgacct tgccagctcc agcagccttc tggtccactg ctttgatgac
                                                                        180
acccaccgca actgtctgtc tcatatcacg aacagcaaag cgacccaaag gtggatagtc
                                                                        240
tgagaagete teaacacaca tgggettgee aggaaceata teaacaatgg geageateae
                                                                        300
cagacttcaa gaatttaagg gccatcttcc agctttttac cagaacggcg atcaatcttt
                                                                        360
toottcaget cagcaaactt gcatgcaatg tgageeg
                                                                        397
      <210> 187
      <211> 584
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(584)
      \langle 223 \rangle n = A, T, C or G
      <400> 187
tegageggee geeegggeag gteeagaggg etgtgetgaa gtttgetget geeactggag
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ccactccaat tgctggccgc ttcactcctg gaaccttcac taaccagate caggcagcct
                                                                        120
teegggagee aeggettett gtggntaetg acceeaggge tgaccaecag ceteteaegg
                                                                        180
aggeatetta tgttaaceta cetaceattg cgctgtgtaa cacagattet cetetgeget
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atgtggacat tgccatccca tgcaacaaca agggagctca ctcagngggg tttgatgtgg
                                                                        300
                                                                        360
tggatgctgg ctcgggaagt tctgcgcatg cgtggcacca tttcccgtga acacccatgg
                                                                        420
gangneatge etgatetgga ettetaeaga gateetgaag agattgaaaa agaagaacag
gctqnttqct ganaaaqcaa gtgaccaagg angaaatttc anggqtqaaa ngqactqctc
                                                                        480
cogetectga atteactget acteaacctg angntgcaga etggtettga aggngnacan
                                                                        540
gggccctctg ggcctattta agcancttcg gtcgcgaaca cgnt
                                                                        584
      <210> 188
      <211> 579
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(579)
      <223> n = A, T, C or G
      <400> 188
agcgtgngtc gcggccgagg tgctgaatag gcacagaggg cacctgtaca ccttcagacc
                                                                         60
agtctgcaac ctcaggctga gtagcagtga actcaggagc gggagcagtc cattcaccct
                                                                        120
gaaattcctc cttggncact gccttctcag cagcagcctg ctcttcttt tcaatctctt
                                                                        180
caggatetet gtagaagtac agateaggea tgaceteeca tgggtgttea egggaaatgg
                                                                        240
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BNSDOCID: <WO_____0036107A2_I_>

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tgccacgcat gcgcagaact tcccgagcca gcatccacca catcaaaccc actgagtgag
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ctcccttgtt gttgcatggg atgggcaatg tccacatagc gcagaggaga atctgtgtta
                                                                        360
cacagogoaa tggtaggtag gttaacataa gatgootoog ogagaagotg qtqqtcaqoo
                                                                        420
ctggggtcaa gtaaccacaa gaagccgtgg ctcccggaag gctgcctgga tctggttagt
                                                                        480
gaaggntcca ggagtgaagc ggccaacaat tggagtggct tcagtggcaa gcagcaaact
                                                                        540
tcagcacaag ccctctggac ctgcccggcg gccgctcga
                                                                        579
      <210> 189
      <211> 374
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature *
     <222> (1)...(374)
    \sim <223> n = A, T, C or G
      <400> 189
tegageggee geeegggeag gteeatttte teeetgaegg neceaettet etceaatett
                                                                         60
gtagttcaca ccattgtcat ggcaccatct agatgaatca catctgaaat gaccacttcc
                                                                        120
aaagcctaag cactggcaca acagtttaaa gcctgattca gacattcgtt cccactcatc
                                                                        180
tccaacggca taatgggaaa ctgtgtaggg gtcaaagcac gagtcatccg taggttggtt
                                                                        240
caageetteg ttgacagagt tgeecaeggt aacaaceten teecegaace ttatgeetet
                                                                        300
gctgggcttt cagngcctcc actatgatgn tgtagggggg cacctctggn gangacctcg
                                                                        360
gccgcgacca cgct
                                                                        374
      <210> 190
      <211> 373
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(373)
      <223> n = A, T, C or G
      <400> 190
agcgtggtcg cggccgaggt cctcaccaga ggtgccacct acaacatcat agtggaggca
                                                                         60
ctgaaagacc agcagaggca taaggctcgg gaagaggttg ttaccgtggg caactctgtc
                                                                       120
aacgaagget tgaaccaace tacggatgae tegtgetttg acceetacae agttteceat
                                                                       180
tatgccgttg gagatgagtg ggaacgaatg tctgaatcag gctttaaact gttgtgccag
                                                                       240
tgcttangct ttggaagtgg gtcatttcag atgtgattca tctagatggt gccatgacaa
                                                                       300
tggngngaac tacaagattg gagagaagtg gnaccgncag ggagaaaatg gacctgcccg
                                                                       360
ggcggccgct cga
                                                                       373
     <210> 191
     <211> 354
      <212> DNA
      <213> Homo sapien
     <220>
     <221> misc feature
     <222> (1)...(354)
     <223> n = A, T, C or G
```

```
<400> 191
agcgtggtcg cggccgaggt ccacatcggc agggtcggag ccctggccgc catactcgaa
                                                                         60
ctggaatcca tcggtcatgc tctcgccgaa ccagacatgc ctcttgtcct tggggttctt
                                                                        120
gctgatgtac cagttettet gggccacact gggctgagtg gggtacacge aggtetcace
                                                                        180
agtotocatg ttgcagaaga ctttgatggc atccaggntg caaccttggt tggggtcaat
                                                                        240
ccagtactct ccactcttcc agccagagtg gcacatcttg aggtcacggc aggtgcggnc
                                                                        300
gggggntttt gcggctgccc tctggncttc ggntgtnctc natctgctgg ctca
                                                                        354
      <210> 192
      <211> 587
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(587)
      <223> n = A, T, C or G
      <400> 192
tegageggee geeegggeag gtetegeggt egeactggtg atgetggtee tgttggteee
                                                                         60
eceggeeete etggaeetee tggeeeeet ggteeteesa gegetggttt egaetteage
                                                                        120
ttcctgcccc agccacctca agagaaggct cacgatggtg gccgctacta ccgggctgat
                                                                        180
gatgccaatg tggttcgtga ccgtgacctc gaggtggaca ccaccctcaa gagcctgagc
                                                                        240
cagcagatcg agaacatccg gagcccagag ggcagncgca agaaccccgc ccgcacctgc
                                                                        300
cgtgacctca agatgtgcca ctctgactgg aagagtggag agtactggat tgaccccaac
                                                                        360
caagetgcaa cetggatgce atcaaagtet tetgcaacat ggagactggt gagacetgeg
                                                                        420
tgtaccccac tcagcccagt gtggcccaaa agaactggta catcagcaag aaccccaagg
                                                                       . 480
acaagaagca tgtctggttc ggcgagaaca tgaccgatgg attccagttc gagtatggcg
                                                                       540
ggcagggctc cgaccctgcc gatggggacc ttggccgcga acacgct
                                                                       587
      <210> 193
      <211> 98
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(98)
      <223> n = A, T, C or G
      <400> 193
agcgtggnng cggccgaggt ataaatatcc agnccatatc ctccctccac acgctganag
                                                                        60
atgaagctgt ncaaagatct cagggtggan aaaaccat
                                                                        98
      <210> 194
      <211> 240
      <212> DNA
      <213> Homo sapien
      <400> 194
tegageggee geeegggeag gteetteaga ettggaetgt gteacaetge eaggetteea
                                                                        60
gggctccaac ttgcagacgg cctgttgtgg gacagtctct gtaatcgcga aagcaaccat
                                                                       120
ggaagacetg ggggaaaaca ccatggtttt atccaccetg agatetttga acaacttcat
                                                                       180
ctctcagcgt gcggagggag gctctggact ggatatttct acctcqqccq cqaccacqct
                                                                       240
```

```
<210> 195
   <211> 400
    <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(400)
      <223> n = A, T, C or G
      <400> 195
cgagcgggcg accgggcagg tncagactcc aatccanana accatcaagc cagatgtcag
                                                                        60
aagctacacc atcacaggtt tacaaccagg cactgactac aaganctacc tgcacacctt
                                                                       120
quatgacaat gctcggagct cccctgtggt catcgacgcc tccactgcca ttgatgcacc
                                                                       180
atccaacctg cgtttcctgg ccaccacacc caattccttg ctggtatcat ggcagccgcc
                                                                       240
acgigecagg attaccggta catcatenag tatganaage etgggeetee teccagagaa
                                                                       300
gnggtccctc ggccccgccc tgntgtccca naggntacta ttactgngcc ngcaaccggc
                                                                       360
aaccgatatc nattttgnca ttggccttca acaataatta
                                                                       400
      <210> 196
      <211> 494
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(494)
      <223> n = A, T, C or G
      <400> 196
agogtggttc goggoogang tootgtoaga gtggoactqq taqaaqttoc aqqaaccotq
                                                                        60
aactgtaagg gttcttcatc agngccaaca ggatgacatg aaatgatgta ctcaqaagtg
                                                                       120
tectggaatg gggeecatga gatggttgte tgagagagag ettettgnee tgtettttte
                                                                       180
cttccaatca ggggctcgct cttctgatta ttcttcaggg caatgacata aattgtatat
                                                                       240
togggtocog gntocaggoo agtaatagta noctotqtga caccagggog gnqocqaggg
                                                                       300
accacttctc tgggaggaga cccaggcttc tcatacttga tgatgtaacc ggtaatcctg
                                                                       360
gcacgtggcg gctgccatga taccagcaag gaattggggt gtggtggcca ggaaacgcag
                                                                       420
gttggatggn gcatcaatgg cagtggaggc cgtcgatgac cacaggggga gctccgacat
                                                                       480
tgtcattcaa ggtg
                                                                       494
      <210> 197
      <211> 118
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(118)
      <223> n = A, T, C or G
      <400> 197
agegtggneg eggeegaggt geagegeggg etgtgeeace ttetgetete tgeecaacqa
                                                                        60
taaggaggt neetgeeec aggagaacat taactnteec cageteggee tetgeegg
                                                                       118
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<210> 198

```
<211> 403
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(403)
      <223> n = A, T, C or G
      <400> 198
tcgagcggcc gcccgggcag gttttttttg ctgaaagtgg ntactttatt ggntgggaaa
                                                                         60
gggagaagct gtggtcagcc caagagggaa tacagagncc cgaaaaaggg gagggcaggt
                                                                       120
gggctggaac cagacgcagg gccaggcaga aactttctct cctcactgct cagcctggtg
                                                                       180
gtggctggag ctcanaaatt gggagtgaca caggacacct tcccacagcc attgcggcgg
                                                                       240
cattteatet ggecaggaea etggetgtee acetggeaet ggteeegaea gaageeegag
                                                                       300
ctggggaaag ttaatgttca cctgggggca ggaaccctcc ttatcattgn gcagagagca
                                                                       360
gaaggtggca cagcccgcgc tgcacctcgg ccgcgaccac gct
                                                                       403
      <210> 199
      <211> 167
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(167)
      <223> n = A, T, C or G
      <400> 199
tcgagcggcc gcccgggcag gtccaccata agtcctgata caaccacgga tgagctgtca
                                                                        60
ggagcaaggt tgatttcttt cattggtccg gncttctcct tgggggncac ccgcactcga
                                                                       120
tatccagtga gctgaacatt gggtggcgtc cactgggcgc tcaggct
                                                                       167
      <210> 200
      <211> 252
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(252)
      <223> n = A, T, C or G
      <400> 200
tcgagcggtt cgcccgggca ggtccaccac acccaattcc ttgctggtat catggcagcc
                                                                        60
gccacgtgcc aggattaccg gctacatcat caagtatgag aagcctgggt ctcctcccag
                                                                       120
agaageggte ecteggeece geeetggtgt cacagagget actattactg geetggaace
                                                                       180
gggaaccgaa tatacaattt atgtcattgn cctgaagaat aatcannaan agcgancccc
                                                                       240
tgattggaag ga
                                                                       252
      <210> 201
      <211> 91
      <212> DNA
      <213> Homo sapien
```

```
<400> 201
agcgtggtcg cggccgaggt tgtacaagct ttttttttt tttttttt tttttttt
                                                                        60
tttttttt ttttttttt tttttt ttttttt t
                                                                        91
      <210> 202
      <211> 368
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(368)
      <223> n = A, T, C or G
      <400> 202
tcgagcggnc gcccgggcag gtctgccaac accaagattg gcccccgccg catccacaca
                                                                        60
qtccqtqtqc qqqqaqqtaa caaqaaatac cqtqccctqa qqttqqacqt qqqqaatttc
                                                                       120
tcctggggct cagagtgttg tactcgtaaa acaaggatca tcgatgttgt ctacaatgca
                                                                       180
totaataacg agotggttcg taccaagaco otggtgaaga attgcatogt gotcatogac
                                                                       240
agcacaccgt accgacagtg gtacgagtcc cactatgcgc tgcccctggg ccgcaagaag
                                                                       300
ggagccaagc tgactcctga ggaagaagag attttaaaca aaaaacgatc taanaaaaaa
                                                                       360
aaaacaat
                                                                       368
      <210> 203
      <211> 340
      <212> DNA
      <213> Homo sapien
      <400> 203
agcgtggtcg cggccgaggt gaaatggtat tcagcttcct ggcacttctg gtcagcaacc
                                                                        60
cagtgttggg caacaaatga tctttgagga acatggtttt aggcggacca caccgcccac
                                                                       120
aacggccacc cccataaggc ataggccaag accatacccg ccgaatgtag gacaagaagc
                                                                       180
totototoag acaaccatot catgggcocc attocaggac acttotgagt acatcattto
                                                                       240
atgtcatcct gttggcactg atgaagaacc cttacagttc agggttcctg qaacttctac
                                                                       300
cagtgccact ctgacaggac etgcccgggc ggccgctcga
                                                                       340
      <210> 204
      <211> 341
      <212> DNA
      <213> Homo sapien
      <400> 204
togagoggco geoogggcag gtootgtoag agtggcactg gtagaagtto caggaaccet
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qaactqtaag ggttcttcat cagtgccaac aggatgacat gaaatgatgt actcagaagt
                                                                       120
qtcctggaat ggggcccatg agatggttgt ctgagagaga gcttcttgtc ctacattcgg
                                                                       180
cgggtatggt cttggcctat gccttatggg ggtggccgtt gtggqcqqtq tqqtccqcct
                                                                       240
aaaaccatgt tootcaaaga toatttgttg cocaacactg ggttgctgac cagaagtgcc
                                                                       300
aggaagetga ataccattte accteggeeg egaceaeget a
                                                                       341
      <210> 205
      <211> 770
      <212> DNA
      <213> Homo sapien
      <220>
```

```
<221> misc feature
      <222> (1)...(770)
      <223> n = A, T, C or G
      <400> 205
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togtaccact gtoggtacgg tgtgctgtog atgagcacga tgcaattott caccagggto
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ttqqtacqaa ccaqctcqtt attaqatqca ttqtaqacaa catcqatqat ccttqtttta
                                                                       180
cgagtacaac actctgagcc ccaggagaaa ttccccacgt ccaacctcag ggcacggtat
                                                                       240
ttettgttac eteccegeae aeggaetgtg tggatgegge gggggeeaag etgaeteetg
                                                                       300
aggaagaaga gattttaaac aaaaaacgat ctaaaaaaat tcagaagaaa tatgatgaaa
                                                                       360
ggaaaaagaa tgccaaaatc agcagtctcc tggaggagca gttccagcag ggcaagcttc
                                                                       420
ttgcgtgcat cgcttcaagg ccgggacagt gtgaccgagc agatggctat gtgctagagg
                                                                       480
gcaaagaagt ggagttctat cttaagaaaa tcagggccca gaatggtgng tcttcaacta
                                                                       540
atccaaaggg gagtttcaga ccagtgcaat cagcaaaaac attgatactg ntggccaaat
                                                                       600
ttattggtgc agggcttgca cantangann ggctgggtct tggggcttgg attggnacaa
                                                                       660
getttggcag cettttettt ggttttgcca aaaacetttt gntgaagang anacetnggg
                                                                       720
cggacccctt aaccgattcc acnccnggng gcgttctang gncccncttg
                                                                       770
      <210> 206
      <211> 810
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(810)
      <223> n = A, T, C or G
      <400> 206
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                                                                        60
aggetgecaa agaetgttee aataceagea eeagaaceag eeacteetae tgttgeagea
                                                                       120
cctgcaccaa taaatttggc agcagtatca atgtctctgc tgattgcact ggtctgaaac
                                                                       180
tccctttgga ttagctgaga cacaccattc tgggccctga ttttcctaag atagaactcc
                                                                       240
aactetttge cetetageae atagecatet geteggteae actgteeegg cettgaageg
                                                                      -300
atgcacgcaa gaagcttgcc ctgctggaac tgctcctcca ggagactgct gattttggca
                                                                       360
ttctttttcc tttcatcata tttcttctga atttttttag atcgttttt gtttaaaatc
                                                                       420
tettetteet caggagteag ettggeece geegeateea cacagteegt gtgegggag
                                                                       480
gtaacaagaa ataccgtgcc ctgaggttgg acgtggggaa tttctcctgg ggctcagagt
                                                                       540
ggtgtactcg taaaacaagg atcatcgatg gtgnctacaa tgcatctaat aacqaqctqq
                                                                       600
gtcggaccca aagaacctgg ngaanaaatg gatcgnctca tcgacaggac accgtacccg
                                                                       660
acaggggnac ganteceact atgegettge ecetgggeeg caanaaagga aaactgeeeg
                                                                       720
ggcggccntc gaaagcccaa ttntggaaaa aatccatcac actgggnggc cngtcgagca
                                                                       780
tgcatntana ggggcccatt ccccctnann
                                                                       810
      <210> 207
      <211> 257
      <212> DNA
      <213> Homo sapien
      <400> 207
tegageggee geeegggeag gteeceaace aaggetgeaa eetggatgee atcaaagtet
                                                                        60
tctgcaacat ggagactggt gagacctgcg tgtaccccac tcagcccagt gtggcccaga
                                                                       120
agaactggta catcagcaag aaccccaagg acaagaggca tgtctggttc ggcgagagca
                                                                       180
tgaccgatgg attccagttc gagtatggcg gccagggctc cgaccctgcc gatgtggacc
                                                                       240
```

```
tcggccgcga ccacgct
                                                                        257
      <210> 208
      <211> 257
      <212> DNA
      <213> Homo sapien
      <400> 208
agcgtggtcg cggccgaggt ccacatcggc agggtcggag ccctggccgc catactcgaa
                                                                        60
ctggaatcca tcggtcatgc tctcgccgaa ccagacatgc ctcttgtcct tggggttctt
                                                                        120
gctgatgtac cagttettet gggccacact gggctgagtg gggtacacge aggtetcace
                                                                        180
agtctccatg ttgcagaaga ctttgatggc atccaggttg cagccttggt tggggacctg
                                                                        240
cccgggcggc cgctcga
                                                                        257
      <210> 209
      <211> 747
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(747)
      <223> n = A, T, C or G
      <400> 209
tegageggee geeegggeag gtecaceaea eccaatteet tgetggtate atggeageeg
                                                                        60
ccacgtgcca ggattaccgg ctacatcatc aagtatgaga agcctgggtc tcctcccaga
                                                                       120
gaagtggtcc ctcggccccg ccctggtgtc acagaggcta ctattactgg cctggaaccq
                                                                       180
ggaaccgaat atacaattta tgtcattgcc ctgaagaata atcagaagag cgagccctg
                                                                       240
attggaagga aaaagacaga cgagcttccc caactggtaa cccttccaca ccccaatctt
                                                                       300
catggaccag agatettgga tgtteettee acagtteaaa agaceeettt egteaeceae
                                                                       360
cctgggtatg acactggaaa tggtattcag cttcctggca cttctggtca gcaacccagt
                                                                       420
gttgggcaac aaatgatctt tgaggaacat ggntttaggc ggaccacacc gcccacaacg
                                                                       480
gccaccccca taaggcatag gccaagacca tacccgccga atgtaggaca agaagctntn
                                                                       540
thtcanacac cathinateg goodcattcc aggacacttc tgagtacatc attitatghca
                                                                       600
tctgtggcac ttgatgaaaa cccttacagt tcagggttct ggaactttta ccaggcctnt
                                                                       660
tacaggactn ggccggacnc cttaagccna ttncaccctg gggcgttcta nggtcccact
                                                                       720
cgnncactgg ngaaaatggc tactgtn .
                                                                       747
      <210> 210
      <211> 872
      <212> DNA
      <213> Homo sapien
     <220>
     <221> misc feature
      <222> (1)...(872)
     <223> n = A, T, C or G
     <400> 210
agegtggteg eggeegaggt ceactagagg tetgtgtgee attgeecagg eagagtetet
                                                                        60
gcgttacaaa ctcctaggag ggcttgctgt gcggagggcc tgctatggtg tgctgcggtt
                                                                       120
catcatggag agtggggcca aaggctgcga ggttgtggtg tctgngaaac tccnaggaca
                                                                       180
ngagggctaa attccatgaa gtttgtggat ggcctgatga tccacaatcg gagaccctgt
                                                                       240
taactactac cgtctnaccn cctgctgtnc ncccccnttt ctgctnaana catngggntn
                                                                       300
```

```
ntncttgncc ntccttgggt ngaanatnna atngcctncc cnttcntanc nctactngnt
                                                                       360
ccananttgg cctttaaana atconccttg ccttnnncac tgttcanntn tttnntcgta
                                                                       420
aaccctatna nttnnattan atnntnnnnn nctcacccc ctcntcattn anccnatang
                                                                       480
ctnnnaantc cttnanncct cccnccennt ncnctentac tnantncttc tnncccatta
                                                                       540
cnnagetett tentttaana taatgnngee nngetetnea thtetaenat htgnnnaath
                                                                       600
cccccncccc cnancgnntt tttgacctnn naacctcctt tcctcttccc tncnnaaatt
                                                                       660
nennanttee nentteenne nttteggntn nteccatnet ttecannnet teantetane
                                                                       720
nenetneaae ttatttteet nteatecett nttetttaca nneeceetnn tetaetenne
                                                                       780
nnttncatta natttgaaac tnccacnnct anttncctcn ctctacnntt ttattttncg
                                                                       840
ntcnctctac ntaatanttt aatnanttnt cn
                                                                       872
      <210> 211
      <211> 517
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (517)
      <223> n = A, T, C or G
      <400> 211
tcgagcggcc gcccgggcag gtctgccaag gagaccctgt tatgctgtgg ggactggctg
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gggcatggca ggcggctctg gcttcccacc cttctgttct gagatggggg tggtgggcag
                                                                       120
tatctcatct ttgggttcca caatgctcac gtggtcaggc aggggcttct tagggccaat
                                                                       180
cttaccagtt gggtcccagg gcagcatgat cttcaccttg atgcccagca caccctgtct
                                                                       240
gagcaacacg tggcgcacaa gcagtgtcaa cgtagtaagt taacagggtc tccgctqtqq
                                                                       300
atcatcagge catccacaaa cttcatggat ttagccctct gtcctcggag tttcccagac
                                                                       360
accacaacct cgcagccttt ggccccactc tccatqatqa accqcagcac accatagcag
                                                                       420
gccctccgca caagcaagcc ctcctaagaa tttgtaacgc ananactctg ctggcaatgg
                                                                       480
cacacaaacc tctagtggac ctcggncgcg accacgc
                                                                       517
      <210> 212
      <211> 695
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(695)
      <223> n = A, T, C or G
      <400> 212
tegageggee geeegggeag gtetggteea ggatageetg egagteetee tactgetact
                                                                        60
ccagacttga catcatatga atcatactgg ggagaatagt tctgaggacc agtagggcat
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gattcacaga ttccaggggg gccaggagaa ccaggggacc ctggttgtcc tggaatacca
                                                                       180
gggtcaccat ttctcccagg aataccagga gggcctqqat ctcccttqqq qccttqaqqt
                                                                       240
ccttgaccat taggagggcg agtaggagca gttggaggct gtgggcaaac tgcacaacat
                                                                       300
tetecaaatg gaattietgg gttggggeag tetaattett gateegteae atattatgte
                                                                       360
atogcagaga acggatoctg agtoacagao acatatttgg catggttotg gottocagao
                                                                       420
atototatoo gnoataggao tgaccaagat gggaacatoo toottoaaca agottnotgt
                                                                       480
tgtgccaaaa ataatagtgg gatgaagcag accgagaagt anccagctcc cctttttgca
                                                                       540
caaagcntca tcatgtctaa atatcagaca tgagacttct ttgggcaaaa aaggagaaaa
                                                                       600
agaaaaagca gttcaaagta nccnccatca agttggttcc ttgcccnttc agcacccggg
                                                                       660
ccccgttata aaacacctng ggccggaccc ccctt
                                                                       695
```

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<210> 213
      <211> 804
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(804)
      <223> n = A, T, C or G
      <400> 213
agcgtggtcg cggccgaggt gttttatgac gggcccggtg ctgaagggca gggaacaact
                                                                         60
tgatggtgct actttgaact gcttttcttt tctccttttt gcacaaagag tctcatgtct
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gatatttaga catgatgagc tttgtgcaaa aggggagctg gctacttctc gctctgcttc
                                                                       180
atcccactat tattttggca caacaggaag ctgttgaagg aggatgttcc catcttggtc
                                                                        240
agtectatge ggatagagat gtetggaage cagaaccatg ccaaatatgt gtetgtgact
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caggatccgt tctctgcgat gacataatat gtgacgatca agaattagac tgccccaacc
                                                                       360
cagaaattcc atttggagaa tgttgtgcag tttgcccaca gcctccaact gctcctactc
                                                                        420
gecetectaa tggteaagga eeteaaggee eeaagggaga teeaggeeet eetggtatte
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ctgggagaaa tggtgaccet ggtattccag gacaaccagg gtcccctggt tctcctggcc
                                                                       540
cccctggaat cnggngaatc atgccctact ggtcctcaaa ctattctccc anatgattca
                                                                       600
tatgatgtca agtctgggat agcnagtang ganggactcg caggctattc tggaccanac
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ctgccggggg ggcgttcgaa agcccgaatc tgcananntn cnttcacact ggcggccgtc
                                                                       720
gagctgcttt aaaagggcca ttccnccttt agngnggggg antacaatta ctnggcggcg
                                                                       780
ttttanancg cgngnctggg aaat
                                                                       804
      <210> 214
      <211> 594
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(594)
      <223> n = A, T, C or G
      <400> 214
agcgtggtcg cggccgaggt ccacatcggc agggtcggag ccctggccgc catactcgaa
                                                                        60
ctggaatcca tcggtcatgc tctcgccgaa ccagacatgc ctcttgtcct tggggttctt
                                                                       120
getgatgtae cagttettet gggeeacaet gggetgagtg gggtaeaege aggteteaee
                                                                       180
agtctccatg ttgcagaaga ctttgatggc atccaggttg cagccttggt tggggtcaat
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ccagiactet ecaetettee agteagagtg geacatettg aggteaegge aggtgeggge
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ggggttettg eggetgeeet etgggeteeg gatgtteteg atetgetgge teaggetett
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gagggtggtg tecaeetega ggteaeggte aegaaecaea ttggeateat eageeeggta
                                                                       420
gtagcggcca ccatcgtgag ccttctcttg angtggctgg ggcaggaact gaagtcgaaa
                                                                       480
ccaqcqctgg gaggaccagg gggaccaana ggtccaggaa gggcccgggg gggaccaaca
                                                                       540
ggaccagcat caccaagtge gaccegegag aacctgeeeg geegneeget egaa
                                                                       594
      <210> 215
      <211> 590
      <212> DNA
      <213> Homo sapien
      <220>
```

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<221> misc feature
      <222> (1)...(590)
      <223> n = A, T, C or G
      <400> 215
tegagegnne geeegggeag gtetegeggt egeaetggtg atgetggtee tgttggtee
                                                                         60
eceggeeete etggaeetee tggteeecet ggteeteeca gegetggttt egaetteage
                                                                        120
ttcctgcccc agccacctca agagaaggct cacgatggtg gccgctacta ccgggctgat
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gatgccaatg tggttcgtga ccgtgacctc gaggtggaca ccaccctcaa gagcctgagc
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cagcagateg agaacateeg gageecagag ggeageegea agaaceeege eegeacetge
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cgtgacctca agatgtgcca ctctgactgg aagagtggag agtactggat tgaccccaac
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caaggetgea acctggatge cateaaagte ttetgeaaca tggagaetgg tgagaeetge
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gtgtacccca ctcagcccag tgtggcccag aagaactggt acatcagcaa gaaccccaag
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gacaagagge atgtetggtt eggegagage atgacegatg gatteeagtt egagtatgge
                                                                       540
ggccagggct cccaccctgc cgatgtggac ctccggccgc gaccaccctt
                                                                        590
      <210> 216
      <211> 801
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(801)
      <223> n = A, T, C or G
      <400> 216
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gtgaagatgg tcaccctgga aaacccggac gacctggtga gagaggagtt gttggaccac
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agggtgctcg tggtttccct ggaactcctg gacttcctgg cttcaaaggc attaggggac
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acaatggtet ggatggattg aagggacage eeggtgetee tggtgtgaag ggtgaacetg
                                                                       240
gtgcccctgg tgaaaatgga actccaggtc aaacaggagc ccgtgggctt cctggtgaga
                                                                       300
gaggaccgtg ttggtgcccc tggcccanac ctcggccgcg accacgctaa gcccgaattt
                                                                       360
ccagcacact ggnggccgtt actantggat ccgagctcgg taccaagctt ggcgtaatca
                                                                       420
tggtcatagc tgtttcctgn gtgaaattgt tatccgctca caatttcaca cancatacga
                                                                       480
agccggaaag cataaagtgt aaagccttgg ggtgctaatg agtgagctaa ctcncattaa
                                                                       540
attgcgttgc gctcactgcc cgcttttcca nnngggaaac cntggcntng ccngcttgcn
                                                                       600
ttaantgaaa tccgccnacc cccggggaaa agncggtttg cngtattggg gcnctttttc
                                                                       660
cettteeteg gnttaettga nttantggge tttggnegnt tegggttgng geganenggt
                                                                       720
tcaacntcac nccaaaggng gnaanacggt tttcccanaa tccgggggnt ancccaangn
                                                                       780
aaaacatnng ncnaangggc t
                                                                       801
      <210> 217
      <211> 349
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(349)
      <223> n = A, T, C or G
      <400> 217
agegtggttn geggeegagg tetgggeeag gggeaceaae aegteetete teaceaggaa
                                                                        60
gcccacgggc tectgtttga cetggagtte catttteace aggggcacea ggtteaceet
                                                                       120
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tcacaccagg agcaccgggc tgtcccttca atccatncag accattgtgn cccctaatgc
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ctttgaagcc aggaagtcca ggagttccag ggaaaccacc gagcaccctg tggtccaaca
                                                                       240
actoctotot caccagging toogggitti coagggingac catoticaco agoctigoca
                                                                       300
ggaggaccag caggaccagc gttaccaacc tgcccgggcg gccgctcga
                                                                       349
      <210> 218
      <211> 372
      <212> DNA
      <213> Homo sapien
      <400> 218
tegageggee geeegggeag gtecatttte teeetgaegg teeeacttet etecaatett
                                                                        60
gtagttcaca ccattgtcat ggcaccatct agatgaatca catctgaaat gaccacttcc
                                                                       120
aaageetaag caetggeaca acagtttaaa geetgattea gaeattegtt eccaeteate
                                                                       180
tccaacggca taatgggaaa ctgtgtaggg gtcaaagcac gagtcatccg taggttggtt
                                                                       240
caageetteg ttgacagagt tgeceaeggt aacaaeetet teeegaaeet tatgeetetg
                                                                       300
ctggtctttc agtgcctcca ctatgatgtt gtaggtggca cctctggtga ggacctcggc
                                                                       360
cgcgaccacg ct
                                                                       372
      <210> 219
      <211> 374
      <212> DNA
      <213> Homo sapien
      <400> 219
agegtggteg eggeegaggt ceteaceaga ggtgeeacet acaacateat agtggaggea
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ctgaaagacc agcagaggca taaggttcgg gaagaggttg ttaccgtggg caactctgtc
                                                                       120
aacgaagget tgaaccaace tacggatgae tegtgetttg acceetacae agttteecat
                                                                       180
tatgccgttg gagatgagtg ggaacgaatg tctgaatcaq qctttaaact qttqtqccaq
                                                                       240
tgcttaggct ttggaagtgg tcatttcaag atgtgattca tctagatggt gccatgacaa
                                                                       300
tggtgtgaac tacaagattg gagagaagtg ggaccgtcag ggagaaaatg gacctgcccg
                                                                       360
ggccggccgc tcga
                                                                       374
      <210> 220
      <211> 828
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(828)
      <223> n = A, T, C or G
      <400> 220
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geggeagttg teacagegee ageceegetg geetecaaag catgtgeagg ageaaatgge
                                                                       120
accgagatat teettetgee actgttetee tacgtggtat gtetteecat categtaaca
                                                                       180
cgttgcctca tgagggtcac acttgaattc tccttttccg ttcccaagac atgtgcagct
                                                                       240
catttggctg gctctatagt ttggggaaag tttgttgaaa ctgtgccact qacctttact
                                                                       300
tecteettet etaetggage titegtaeet tecaettetg etgttggtaa aatggtggat
                                                                       360
cttctatcaa tttcattgac agtacccact tctcccaaac atccagggaa atagtgattt
                                                                       420
cagagcgatt aggagaacca aattatgggg cagaaataag gggcttttcc acaggttttc
                                                                       480
ctttggagga agatttcagt ggtgacttta aaagaatact caacagtgtc ttcatcccca
                                                                       540
tagcaaaaga agaaacngta aatgatggaa ngcttctgga gatgccnnca tttaagggac
                                                                       600
neccagaact teaceateta caggacetae tteagtttae annaagneae atantetgae
                                                                       660
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tcanaaagga cccaagtagc nccatggnca gcactttnag cctttcccct ggggaaaann
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ttacnttctt aaancctngg cenngacece ettaagneea aattntggaa aantteentn
                                                                       780
cnnctggggg gcngttcnac atgcntttna agggcccaat tnccccnt
                                                                       828
      <210> 221
      <211> 476
      <212> DNA
      <213> Homo sapien
      <400> 221
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teteeggetg eccattgete teccaeteca eggegatgte getgggatag aageetttga
                                                                       120
ccaggcaggt caggctgacc tggttcttgg tcatctcctc ccgggatggg ggcagggtgt
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acacetgtgg ttctcggggc tgccctttgg ctttggagat ggttttctcg atgggggctg
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ggagggettt gttggagaee ttgeaettgt acteettgee atteageeag teetggtgea
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ggacggtgag gacgctgacc acacggtacg tgctgttgta ctgctcctcc cgcggctttg
                                                                       360
tettggcatt atgeacetee acgeegteea egtaceagtt gaacttgace teagggtett
                                                                       420
cgtggctcac gtccaccacc acgcatgtaa cctcagacct cggccgcgac cacgct
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      <211> 477
      <212> DNA
      <213> Homo sapien
      <400> 222
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ccctgaggtc aagttcaact ggtacgtgga cggcgtggag gtgcataatg ccaagacaaa
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gccgcgggag gagcagtaca acagcacgta ccgtgtggtc agcgtcctca ccgtcctgca
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ccaggactgg ctgaatggca aggagtacaa gtgcaaggtc tccaacaaag ccctcccagc
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ccccatcgag aaaaccatct ccaaagccaa agggcaagcc ccgagaacca caggtgtaca
                                                                       300
ccctgcccc atcccgggag gagatgacca agaaccaggt cagcctgacc tgcctggtca
                                                                       360
aaggetteta teecagegae ategeegtgg agtgggagag caatgggeag eeggagaaca
                                                                       420
actacaagac cacgcctccc gtgctggact ccgacacctg cccgggcggc cgctcga
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      <210> 223
      <211> 361
      <212> DNA
      <213> Homo sapien
      <400> 223
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ggtacagage teegatgggt gaaaceattg acatagagae tgteeetgte eagggtgtag
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gggcccaget cagtgatgee gtgggtcage tggctcaget tecagtacag cegetetetg
                                                                       180
tccagtccag ggcttttggg gtcaggacga tgggtgcaga cagcatccac tctggtggct
                                                                       240
gccccatcct tetcaggeet gageaaggte agtetgeaac cagagtacag agagetgaca
                                                                       300
ctggtgttct tgaacaaggg cataagcaga ccctgaagga cacctcggcc gcgaccacgc
                                                                       360
                                                                       361
      <210> 224
      <211> 361
      <212> DNA
      <213> Homo sapien
      <400> 224
agcgtggtcg cggccgaggt gtccttcagg gtctgcttat gcccttgttc aagaacacca
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gtgtcagctc tctgtactct ggttgcagac tgaccttgct caggcctgag aaggatgggg
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cagecaccag agtggatget gtetgeacce ategteetga ceccaaaage eetggactgg
                                                                       180
acagagageg getgtaetgg aagetgagee agetgaeeea eggeateaet gagetgggee
                                                                       240
ectacaceet ggacagggae agtetetatg teaatggttt cacceategg agetetgtae
                                                                       300
ccaccaccag caccggggtg gtcagcgagg agccattcaa cctgcccggg cggccgctcg
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      <211> 766
      <212> DNA
      <213> Homo sapien
      <220>
     --<221> misc feature
      <222> (1)...(766)
      <223> n = A, T, C or G
      <400> 225
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actgtaaggg ttcttcatca gtgccaacag gatgacatga aatgatgtac tcagaagtgt
                                                                       120
cctggaatgg ggcccatgag atggttgtct gagagagagc ttcttgtcct acattcggcg
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ggtatggtčt tggcctatgc cttatggggg tggccgttgt gggcggtgtg gtccgcctaa
                                                                       240
aaccatgttc ctcaaagatc atttgttgcc caacactggg ttgctgacca gaagtgccag
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gaagctgaat accatttcca gtgtcatacc cagggtgggt gacgaaaggg gtcttttgaa
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ctgtggaagg aacatccaag atctctggtc catgaagatt ggggtgtgga agggttacca
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gttggggaag ctcgtctgtc tttttccttc caatcagggg ctcgctcttc tgattattct
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tcagggcaat gacataaatt gtatattcgg tcccggttcc aggccagtaa tagtagcctc
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tgtgacacca gggcggggcc gagggaccct tctnttggaa gagaccagct tctcatactt
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gatgatgagn ccggtaatcc tggcacgtgg nggttgcatg atnccaccaa ggaaatnggn
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gggggnggac ctgcccggcg gccgttcnaa agcccaattc cacacacttg gnggccgtac
                                                                       720
tatggatccc actengtcca acttggngga atatggcata actttt
                                                                       766
      <210> 226
      <211> 364
      <212> DNA
      <213> Homo sapien
      <400> 226
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                                                                        60
tecacagaca aggecaggae tegtttgtae eegttgatga tagaatgggg taetgatgea
                                                                       120
acagttgggt agccaatctg cagacagaca ctggcaacat tgcggacacc ctccaggaag
                                                                       180
cgagaatgca gagtttcctc tgtgatatca agcacttcag ggttgtagat gctgccattg
                                                                       240
tcgaacacct gctggatgac cagcccaaag gagaaggggg agatgttgag catgttcagc
                                                                       300
agegtggett egetggetee eactitigtet eeagtetiga teagaceteg geegegaeea
                                                                       360
cgct
                                                                       364
      <210> 227
      <211> 275
      <212> DNA
      <213> Homo sapien
      <400> 227
agcgtggtcg cggccgaggt ctgtcctaca gtcctcagga ctctactccc tcagcagcgt
                                                                        60
ggtgaccgtg ccctccagca acttcggcac ccagacctac acctgcaacg tagatcacaa
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gcccagcaac accaaggtgg acaagagagt tgagcccaaa tcttgtgaca aaactcacac
                                                                       180
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```
atgcccaccg tgcccagcac ctgaactcct ggggggaccg tcagtcttcc tcttcccccg
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catcccctt ccaaacctgc ccgggcggcc gctcg
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      <210> 228
      <211> 275
      <212> DNA
      <213> Homo sapien
      <400> 228
cgagcggccg cccgggcagg tttggaaggg ggatgcgggg gaagaggaag actgacggtc
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ccccaggag ttcaggtgct gggcacggtg ggcatgtgtg agttttgtca caagatttgg
                                                                       120
getcaactet ettgtecace ttggtgttge tgggettgtg atetacgttg eaggtgtagg
                                                                       180
tctgggtgcc gaagttgctg gagggcacgg tcaccacgct gctgagggag tagagtcctg
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aggactgtag gacagacctc ggccgcgacc acgct
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      <210> 229
      <211> 40
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (40)
      <223> n = A, T, C or G
      <400> 229
nggnnggtcc ggncngncag gaccactcnt cttcgaaata
                                                                       . 40
      <210> 230
      <211> 208
      <212> DNA
      <213> Homo sapien
      <400> 230
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gaagegeaga tetgttttaa agteetgage aatttetege accagaeget ggaagggaag
                                                                       120
tttgcgaatc agaagttcag tggacttctg ataacgtcta atttcacqqa qcqccacagt
                                                                       180
accaggacct gcccgggcgg ccgctcga
                                                                       208
      <210> 231
      <211> 208
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(208)
      <223> n = A, T, C or G
      <400> 231
tcgagcggcc gcccgggcag gtcctggtac tgnggcgctc cgtgaaatta gacgttatca
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gaagtccact gaacttctga ttcgcaaact tcccttccag cgtctggtgc gagaaattgc
                                                                       120
tcaggacttt aaaacagatc tgcgcttcca gagcgcagct atcggtgctt tgcaggaggc
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aagtgaggac ctcggccgcg accacgct
                                                                       208
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<210> 232
      <211> 332
      <212> DNA
      <213> Homo sapien
      <400> 232
togagoggco gooogggcag gtocacatog goagggtogg agoootggco gooatactog
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aactggaatc catcggtcat getetegeeg aaccagacat geetettgte ettggggtte
                                                                       120
ttgctgatgt accagttctt ctgggccaca ctgggctgag tggggtacac gcaggtctca
                                                                       180
ccagteteca tgttgcagaa gaetttgatg gcatecaggt tgcageettg gttggggtca
                                                                       240
atccagtact ctccactctt ccagtcagag tggcacatct tgaggtcacg gcaggtgcgg
                                                                       300
gcggggttct tgacctcggc cgcgaccacg ct
                                                                       332
      <210> 233
      <211> 415
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(415)
      <223> n = A, T, C or G
      <400> 233
gtgggnttga accentttna netecgettg gtacegaget eggateeact agtaaeqqee
                                                                        60
gccagtgtgc tggaattcgg cttagcgtgg tcgcggccga ggtcaagaac cccgcccgca
                                                                       120
cctgccgtga cctcaagatg tgccactctg actggaagag tggagagtac tggattgacc
                                                                       180
ccaaccaagg ctgcaacctg gatgccatca aagtcttctg caacatggag actggtgaga
                                                                       240
cctgcgtgta cccactcag cccagtgtgg cccagaagaa ctggtacatc agcaagaacc
                                                                       300
ccaaggacaa gaggcatgtc tggttcggcg agagcatgac cgatggattc cagttcgagt
                                                                       360
atggcggcca gggctccgac cctgccgatg tggacctgcc cgggcggccg ctcga
                                                                       415
      <210> 234
      <211> 776
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(776)
      <223> n = A, T, C or G
      <400> 234
agcgtggtcg cggccgaggt ctgggatgct cctgctgtca cagtgagata ttacaggatc
                                                                        60
acttacggag aaacaggagg aaatagccct gtccaggagt tcactgtgcc tgggagcaag
                                                                       120
tctacagcta ccatcagcgg ccttaaacct ggagttqatt ataccatcac tgtgtatgct
                                                                       180
gtcactggcc gtggagacag ccccgcaagc agcaagccaa tttccattaa ttaccgaaca
                                                                       240
gaaattgaca aaccatccca gatgcaagtg accgatgttc aggacaacag cattagtgtc
                                                                       300
aagtggctgc cttcaagttc ccctgttact ggttacagag taaccaccac tcccaaaaat
                                                                       360
ggaccaggac caacaaaaac taaaactgca ggtccagatc aaacagaaat gactattgaa
                                                                       420
ggcttgcagc ccacagtgga gtatgtggtt aagtgtctat gctcagaatc caagcggaga
                                                                       480
gaagtcagcc tctggttcag actgnaagta accaacattg atcgcctaaa ggactggcat
                                                                       540
tcactgatgn ggatgccgat tccatcaaaa ttgnttggga aaacccacag gggcaagttt
                                                                       600
ncangtonag gnggacctac togagocctg aggatggaat cottgactnt toottnnoct
                                                                       660
gatggggaaa aaaaaccttn aaaacttgaa ggacctgccc gggcggccgt ncaaaaccca
                                                                       720
```

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```
attccacccc cttgggggcg ttctatgggn cccactcgga ccaaacttgg ggtaan
                                                                        776
      <210> 235
      <211> 805
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(805)
      <223> n = A, T, C or G
      <400> 235
togagoggee geoogggeag gteettgeag etetgeagtg tettetteae cateaggtge
                                                                         60
agggaatage teatggatte cateeteagg getegagtag gteaccetgt acctggaaac
                                                                        120
ttgcccctgt gggctttccc aagcaatttt gatggaatcg gcatccacat cagtgaatgc
                                                                        180
cagteettta gggegateaa tgttggttae tgeagtetga accagagget gaetetetee
                                                                        240
gcttggattc tgagcataga cactaaccac atactccact gtgggctgca agccttcaat
                                                                        300
agtcatttct gtttgatctg gacctgcagt tttagttttt gttggtcctg gtccatttt
                                                                        360
gggagtggtg gttactctgt aaccagtaac aggggaactt gaaggcagcc acttgacact
                                                                        420
aatgctgttg tcctgaacat cggtcacttg catctgggat ggtttgtcaa tttctgttcg
                                                                        480
gtaattaatg gaaattggct tgctgcttgc ggggcttgtc tccacggcca gtgacagcat
                                                                        540
acacagtgat ggtataatca actccaggtt taagccgctg atggtagctg aaactttgct
                                                                        600
ccaggcacaa gtgaactcct gacagggcta tttcctnctg ttctccgtaa gtgatcctgt
                                                                        660
aatatctcac tgggacagca ggangcattc caaaacttcg ggcgngaccc cctaagccga
                                                                        720
attntgcaat atncatcaca ctggcgggcg ctcgancatt cattaaaagg cccaatcncc
                                                                        780
cctataggga gtntantaca attng
                                                                        805
      <210> 236
      <211> 262
      <212> DNA
      <213> Homo sapien
      <400> 236
tcgagcggcc gcccgggcag gtcacttttg gtttttggtc atgttcggtt ggtcaaagat
                                                                        60
aaaaactaag tttgagagat gaatgcaaag gaaaaaaata ttttccaaag tccatgtgaa
                                                                       120
attgtctccc atttttttgg cttttgaggg ggttcagttt gggttgcttg tctgtttccg
                                                                       180
ggttgggggg aaagttggtt gggtgggagg gagccaggtt gggatggagg gagtttacag
                                                                       240
gaagcagaca gggccaacgt cg
                                                                       262
      <210> 237
      <211> 372
      <212> DNA
      <213> Homo sapien
      <400> 237
agcgtggtcg cggccgaggt cctcaccaga ggtgccacct acaacatcat agtggaggca
                                                                        60
ctgaaagacc agcagaggca taaggttcgg gaagaggttg ttaccgtggg caactctgtc
                                                                       120
aacgaagget tgaaccaace tacggatgae tegtgetttg acceptacae agttteceat
                                                                       180
tatgccgttg gagatgagtg ggaacgaatg tctgaatcag gctttaaact gttgtgccag
                                                                       240
tgcttaggct ttggaagtgg tcatttcaga tgtgattcat ctagatggtg ccatgacaat
                                                                       300
ggtgtgaact acaagattgg agagaagtgg gaccgtcagg gagaaaatgg acctgcccgg
                                                                       360
geggeegete ga
                                                                       372
     <210> 238
```

```
<211> 372
       <212> DNA
       <213> Homo sapien
       <400> 238
 tcgagcggcc gcccgggcag gtccattttc tccctgacgg tcccacttct ctccaatctt
                                                                         60
gtagttcaca ccattgtcat ggcaccatct agatgaatca catctgaaat gaccacttce
                                                                        120
 aaagcctaag cactggcaca acagtttaaa gcctgattca gacattcgtt cccactcatc
                                                                        180
 tccaacggca taatgggaaa ctgtgtaggg gtcaaagcac gagtcatccg taggttggtt
                                                                        240
 caageetteg ttgacagagt tgeecaeggt aacaacetet teeegaacet tatgeetetg
                                                                        300
 ctggtctttc agtgcctcca ctatgatgtt gtaggtggca cctctggtga ggacctcggc
                                                                        360
 cgcgaccacg ct
                                                                        372
       <210> 239
       <211> 720
       <212> DNA /
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1) ... (720)
       <223> n = A,T,C or G
       <400> 239
 tcgagcggcc gcccgggcag gtccaccata agtcctgata caaccacgga tgagctgtca
                                                                         60
 ggagcaaggt tgatttcttt cattggtccg gtcttctcct tggggggtcac ccgcactcga
                                                                        120
 tatccagtga gctgaacatt gggtggtgtc cactgggcgc tcaggcttgt gggtgtgacc
                                                                        180
 tgagtgaact tcaggtcagt tggtgcagga atagtggtta ctgcagtctg aaccagaggc
                                                                        240
 tgactetete egettggatt etgageatag acaetaacea cataeteeae tgtgggetge
                                                                        300
 aagccttcaa tagtcatttc tgtttgatct ggacctgcag ttttagtttt tgttggtcct
                                                                        360
 ggtccatttt tgggagtggt ggttactctg taaccagtaa caggggaact tgaaggcagc
                                                                        420
 cacttgacac taatgctgtt gtcctgaaca tcggtcactt gcatctggga tggtttgnca
                                                                        480
 atttctgttc ggtaattaat ggaaattggc ttgctgcttg cggggctgtc tccacggcca
                                                                        540
 gtgacagcat acacagngat ggnatnatca actccaagtt taaggccctg atggtaactt
                                                                        600
 taaacttgct cccagccagn gaacttccgg acagggtatt tcttctggtt ttccgaaagn
                                                                        660
 gancctggaa tnntctcctt ggancagaag gancntccaa aacttgggcc ggaacccctt
                                                                        720
       <210> 240
       <211> 691
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(691)
       <223> n = A, T, C or G
       <400> 240
 agegtggteg eggeegaggt cetgteagag tggeaetggt agaagtteea ggaaecetga
                                                                         60
actgtaaggg ttcttcatca gtgccaacag gatgacatga aatgatgtac tcagaagtgt
                                                                        120
cctggaatgg ggcccatgag atggttgtct gagagagagc ttcttgtcct acattcggcg
                                                                        180
qqtatggtct tggcctatgc cttatggggg tggccgttgt gggcggtgtg gtccgcctaa
                                                                        240
aaccatgttc ctcaaagatc atttgttgcc caacactggg ttgctgacca gaagtgccag
                                                                        300
gaagctgaat accatttcca gtgtcatacc cagggtgggt gacgaaaggg gtcttttgaa
                                                                        360
ctgtggaagg aacatccaag atctctggtc catgaagatt ggggtgtgga agggttacca
                                                                        420
```

```
gttggggaag ctcgtctgtc tttttccttc caatcagggg ctcgctcttc tgattattct
                                                                         480
tcagggcaat gacataaatt gtatattcgg ttcccggttc caggccagta atagtagcct
                                                                         540
cttgtgacac caggeggggc ccanggacca cttctctggg angagaccca gcttctcata
                                                                         600
cttgatgatg taacceggta atcctgcacg tggcggctgn catgatacca ncaaggaatt
                                                                         660
gggtgnggng gacctgcccg gcggccctcn a
                                                                         691
       <210> 241
      <211> 808
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(808)
      <223> n = A, T, C or G
      <400> 241
agcgtggtcg cggccgaggt ctgggatgct cctgctgtca cagtgagata ttacaggatc
                                                                         60
acttacggag aaacaggagg aaatagccct gtccaggagt tcactgtgcc tgggagcaag
                                                                        120
tetacageta ceateagegg cettaaacet ggagttgatt ataceateae tgtgtatget
                                                                        180
gtcactggcc gtggagacag ccccgcaagc agcaagccaa tttccattaa ttaccgaaca
                                                                        240
gaaattgaca aaccatccca gatgcaagtg accgatgttc aggacaacag cattagtgtc
                                                                        300
aagtggctgc cttcaagttc ccctgttact ggttacagag taaccaccac tcccaaaaat
                                                                        360
ggaccaggac caacaaaaac taaaactgca ggtccagatc aaacagaaat gactattgaa
                                                                        420
ggcttgcagc ccacagtgga gtatgtggtt agtgtctatg ctcagaatcc aagcggagag
                                                                     <sup>13</sup> 480
agtcagcctc tggttcagac tgcagtaacc actattcctg caccaactga cctgaagttc
                                                                        540
actcaggtca cacccacaag cctgagccgc cagtggacac cacccaatgt tcactcactg
                                                                        600
gatatcgagt gcgggtgacc cccaaggaga agacccggac ccatgaaaga aatcaacctt
                                                                        660
qctcctgaca gctcatccgn gggtgtatca ggacttatgg gggactgccc cggcnggccg
                                                                        720
ntcgaaancg aattntgaaa tttccttcnc actgggnggc gnttcgagct tncttntana
                                                                        780
nggcccaatt cncctntagn gggtcgtn
                                                                        808
      <210> 242
      <211> 26
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(26)
      <223> n = A, T, C or G
      <400> 242
agcgtggtcg cggccgaggt cnagga
                                                                         26
      <210> 243
      <211> 697
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
     <222> (1)...(697)
      <223> n = A, T, C or G
```

```
<400> 243
tegageggee geeegggeag gteeaceaea eccaatteet tgetggtate atggeageeg
                                                                        60
ccacgtgcca ggattaccgg ctacatcatc aagtatgaga agcctgggtc tcctcccaga
                                                                       120
gaagtggtcc ctcggccccg ccctggtgtc acagaggcta ctattactgg cctggaaccg
                                                                       180
ggaaccgaat atacaattta tgtcattgcc ctgaagaata atcagaagag cgagccctg
                                                                       240
attggaagga aaaagacaga cgagcttccc caactggtaa cccttccaca ccccaatctt
                                                                       300
catggaccag agatettgga tgtteettee acagtteaaa agacceettt egteacceae
                                                                       360
cctgggtatg acactggaaa tggtattcag cttcctggca cttctggtca gcaacccagt
                                                                       420
gttgggcaac aaatgatctt tgaggaacat ggttttaggc ggaccacacc gcccacaacg
                                                                       480
ggcaccccca taaggnatag gccaagacca taccccgccg aatgtaggac aagaagctct
                                                                       540
ntctcaacaa ccatctcatg ggccccattc caggacactt ctgagtacat catttcatgt
                                                                       600
catcctggtg ggcacttgat gaanaaccct tacagttcag ggttcctgga acttctacca
                                                                       660
gngccacttc tgacagganc ttgggcgnga ccaccct
                                                                       697
      <210> 244
      <211> 373
      <212> DNA
     <213> Homo sapien
      <400> 244
agcgtggtcg cggccgaggt ccattttctc cctgacggtc ccacttctct ccaatcttgt
                                                                        60
agttcacacc attgtcatgg caccatctag atgaatcaca tctgaaatga ccacttccaa
                                                                       120
agcctaagca ctggcacaac agtttaaagc ctgattcaga cattcgttcc cactcatctc
                                                                       180
caacggcata atgggaaact gtgtaggggt caaagcacga gtcatccgta ggttggttca
                                                                       240
agcettegtt gacagagttg eccaeggtaa caacetette ecgaacetta tgeetetget
                                                                       300
ggtctttcag tgcctccact atgatgttgt aggtggcacc tctggtgagg acctgcccgg
                                                                       360
gcggcccgct cga
                                                                       373
      <210> 245
      <211> 307
      <212> DNA
      <213> Homo sapien
      <400> 245
agegtggteg eggeegaggt gtgeeceaga ceaggaatte ggettegaeg ttggeeetgt
                                                                       60
ctgcttcctg taaactccct ccatcccaac ctggctccct cccacccaac caactttccc
                                                                       120
cccaacccgg aaacagacaa gcaacccaaa ctgaaccccc tcaaaagcca aaaaaatggg
                                                                       180
agacaatttc acatggactt tggaaaatat tttttcctt tgcattcatc tctcaaactt
                                                                       240
agtttttatc tttgaccaac cgaacatgac caaaaaccaa aagtgacctg cccgggcggc
                                                                       300
cgctcga
                                                                       307
      <210> 246
      <211> 372
      <212> DNA
      <213> Homo sapien
      <400> 246
togagoggeo geoogggeag gtootcacca gaggtgecac ctacaacate atagtggagg
                                                                        60
cactgaaaga ccagcagagg cataaggttc gggaagaggt tgttaccgtg ggcaactctg
                                                                       120
tcaacgaagg cttgaaccaa cctacggatg actcgtgctt tgacccctac acagtttccc
                                                                       180
attatgccgt tggagatgag tgggaacgaa tgtctgaatc aggctttaaa ctgttgtgcc
                                                                       240
agtgcttagg ctttggaagt ggtcatttca gatgtgattc atctagatgg tgccatgaca
                                                                       300
atggtgtgaa ctacaagatt ggagagaagt gggaccgtca gggagaaaat ggacctcggc
                                                                       360
cgcgaccacg ct
                                                                       372
```

```
<210> 247
      <211> 348
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(348)
      <223> n = A, T, C or G
      <400> 247
tcqaqcqgcc gcccgggcag gtaccggggt ggtcagcgag gagccattca cactgaactt
                                                                        60
caccatcaac aacctgcggt atgaggagaa catgcagcac cctggctcca ggaagttcaa
                                                                       120
caccacggag agggtccttc agggcctgct caggtccctg ttcaagagca ccagtgttgg
                                                                       180
ccctctgtac tctggctgca gactgacttt gctcagacct gagaaacatg gggcagccac
                                                                       240
tggagtggac gccatctgca ccctccgcct tgatcccact ggtnctggac tggacanana
                                                                       300
geggetatae ttgggagetg ancenaacet ttggeggnga encenett
                                                                       348
      <210> 248
      <211> 304
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(304)
      <223> n = A, T, C or G
      <400> 248
gaggactggc tcagctccca gtatagccgc tctctgtcca gtccaggacc agtgggatca
                                                                        60
aggeggaggg tgeagatgge gteeacteea gtggetgeee catgtttete aagtetgage
                                                                       120
aaagncagtc tgcagccaga gtacagaggg ccaacactgg tgctcttgaa cagggacctg
                                                                       180
agcaggccct gaaggaccct ctccgtggtg ttgaacttcc tggagccagg gtgctgcatg
                                                                       240
ttctcctcat accgcaggtt gttgatggtg aagttcagtg tgaatggctc ctcgctgacc
                                                                       300
accc
                                                                       304
      <210> 249
      <211> 400
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(400)
      <223> n = A, T, C or G
      <400> 249
agegtggteg eggeegaggt ceaceaeac caatteettg etggtateat ggeageegee
                                                                        60
acgtgccagg attaccggct acatcatcaa gtatgagaag cctgggtctc ctcccagaga
                                                                       120
agtggtccct cggcccgcc ctggtgtcac agaggctact attactggcc tggaaccggg
                                                                       180
aaccgaatat acaatttatg tcattgccct gaagaataat cagaagagcg agcccctgat
                                                                       240
tggaaggaaa aagacagacg agcttcccca actggtaacc cttccacacc ccaatcttca
                                                                       300
tggaccanan ancttggatn gtcctttcac nggttnaaaa aacccttttc qccccccac
                                                                       360
cttggggatt aaccttggga aanggggatt tnaccnttcc
                                                                       400
```

```
<210> 250
       <211> 400
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(400)
       <223> n = A, T, C or G
      <400> 250
tegageggee geeegggeag gteetgteag agtggeactg gtagaagtte caggaaceet
                                                                         60
gaactgtaag ggttcttcat cagtgccaac aggatgacat gaaatgatgt actcagaagt
                                                                        120
gtcctggaat ggggcccatg agatggttgt ctgagagaga gcttcttgtc ctacattcgg
                                                                        180
cgggtatggt cttggcctat gccttatggg ggtggccgtt gtgggcggtg tggtccgcct
                                                                        240
aaaaccatgt teeteaaaga teatttgttg eccaacactg ggttgetgae cagaagtgee
                                                                        300
aggaagetga ataccattte cagtgtcata eccagggngg gtgaccaaag ggggtenttt
                                                                        360
ngacctggng aaaggaacca tccaaaanct ctgncccatg
                                                                        400
      <210> 251
      <211> 514
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(514)
      <223> n = A, T, C or G
      <400> 251
agcgtggncg cggccgaggt ctgaggatgt aaactcttcc caggggaagg ctgaagtgct
                                                                         60
gaccatggtg ctactgggtc cttctgagtc agatatgtga ctgatgngaa ctgaagtagg
                                                                        120
tactgtagat ggtgaagtct gggtgtccct aaatgctgca tctccagagc cttccatcat
                                                                        180
taccgtttct tcttttgcta tgggatgaga cactgttgag tattctctaa agtcaccact
                                                                        240
gaaatettee tecaaaggaa aacetgtgga aaageeeett atttetgeee cataatttgg
                                                                        300
tteteetaat enetetgaaa teaetattte eetggaangt ttgggaaaaa nngggenace
                                                                        360
tgncantgga aantggatan aaagatccca ccattttacc caacnagcag aaagtgggaa
                                                                        420
nggtaccgaa aagctccaag taanaaaaag gagggaagta aaggtcaagt gggcaccagt
                                                                        480
ttcaaacaaa actttcccca aactatanaa ccca
                                                                        514
      <210> 252
      <211> 501
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(501)
      <223> n = A, T, C or G
      <400> 252
aagcggccgc ccgggcaggn ncagnagtgc cttcgggact gggntcaccc ccaggtctgc
                                                                         60
ggcagttgtc acagegccag ccccgctggc ctccaaagca tgtgcaggag caaatggcac
                                                                        120
cgagatattc cttctgccac tgttctccta cgtggtatgt cttcccatca tcgtaacacg
                                                                        180
ttgcctcatg agggtcacac ttgaattctc cttttccgtt cccaagacat gtgcagctca
                                                                        240
```

```
tttggctggc tctatagttt ggggaaagtt tgttgaaact gtgccactga cctttacttc
                                                                        300
ctecttetet actggagett teegtaeett eeacttetge tgntggnaaa aagggnggaa
                                                                        360
entettatea attteattgg acagtanece netttetnee caaaacatne aagggaaaat
                                                                        420
attgattncn agagcggatt aaggaacaac ccnaattatg ggggccagaa ataaaggggg
                                                                        480
cttttccaca ggtnttttcc t
                                                                        501
      <210> 253
      <211> 226
      <212> DNA
      <213> Homo sapien
      <400> 253
tcqagcggcc gcccgggcag gtctgcaggc tattgtaagt gttctgagca catatgagat
                                                                        60
aacctgggcc aagctatgat gttcgatacg ttaggtgtat taaatgcact tttgactgcc
                                                                        120
atctcagtgg atgacagect teteactgae ageagagate tteetcactg tgecagtggg
                                                                       180
caggagaaag agcatgctgc gactggacct cggccgcgac cacgct
                                                                       226
      <210> 254
      <211> 226
      <212> DNA
      <213> Homo sapien
      <400> 254
agcgtggtcg cggccgaggt ccagtcgcag catgctcttt ctcctgccca ctggcacaqt
                                                                        60
gaggaagatc tctgctgtca gtgagaaggc tgtcatccac tgagatggca gtcaaaagtg
                                                                       120
catttaatac acctaacgta tcgaacatca tagcttggcc caggttatct catatgtgct
                                                                       180
cagaacactt acaatagcct gcagacctgc ccgggcggcc gctcga
                                                                       226
      <210> 255
      <211> 427
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(427)
      <223> n = A, T, C or G
      <400> 255
cgagcggccg cccgggcagg tccagactcc aatccagaga accaccaagc cagatgtcag
                                                                        60
aagctacacc atcacaggtt tacaaccagg cactgactac aagatctacc tgtacacctt
                                                                       120
gaatgacaat gctcggagct cccctgtggt catcgacqcc tccactqcca ttqatqcacc
                                                                       180
atccaacctg cgtttcctgg ccaccacacc caattccttg ctggtatcat ggcagccqcc
                                                                       240
acgtgccagg attaccggct acatcatcaa gtatgagaag cctgggtctc ctcccagaga
                                                                       300
agtggtccct cggccccgcc ctggtgncac agaagctact attactggcc tggaaccggg
                                                                       360
aaccgaatat acaatttatg tcattgccct gaagaataat canaagagcg agcccctgat
                                                                       420
tggaagg
                                                                       427
      <210> 256
      <211> 535
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
```

```
<222> (1)...(535)
      <223> n = A,T;C or G
      <400> 256
agcgtggtcg cggccgaggt cctgtcagag tggcactggt agaagttcca ggaaccctga
                                                                        60
actgtaaggg ttcttcatca gtgccaacag gatgacatga aatgatgtac tcagaagtgt
                                                                       120
cctggaatgg ggcccatgag atggttgtct gagagagagc ttcttgtcct gtcttttcc
                                                                       180
ttccaatcag gggctcgctc ttctgattat tcttcagggc aatgacataa attgtatatt
                                                                       240
cggttcccgg ttccaggcca gtaatagtag cctctgtgac accagggcgg ggccgaggga
                                                                       300
ccacttetet gggaggagae ecaggettet catacttgat gatgtaneeg gtaateetgg
                                                                       360
caccgtggcg gctgccatga taccagcaag gaattgggtg tggtggccaa gaaacgcagg
                                                                       420
ttggatggtg catcaatggc agtggaggcg tcgatnacca caggggagct ccgancattg
                                                                       480
tcattcaagg tggacaggta gaatcttgta atcaggtgcc tggtttgtaa acctg
                                                                       535
      <210> 257
      <211> 544
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(544)
      <223> n = A, T, C or G
      <400> 257
tegageggee geeegggeag gtttegtgae egtgaeeteg aggtggaeae eacceteaag
                                                                        60
agcctgagcc agcagatcga gaacatccgg agcccagagg gcagccgcaa gaaccccgcc
                                                                       120
cqcacctgcc gtgacctcaa gatgtgccac tctgactgga agagtggaga gtactggatt
                                                                       180
gaccccaacc aaggetgeaa eetggatgee atcaaagtet tetgeaacat ggagaetggt
                                                                       240
gagacctgcg tgtaccccac tcagcccagt gtggcccaga agaactggta catcagcaag
                                                                       300
aaccccaagg acaagaagca tgtctggttc ggcgaaagca tgaccgatgg attccagttc
                                                                       360
gagtatggcg gccagggctc cgaccctgcc gatgtggacc tcggccgcga ccacgctaag
                                                                       420
cccgaattcc agcacactgg cggccgttac tagtgggatc cgagcttcgg taccaagctt
                                                                       480
ggcgtaatca tgggncatag ctgtttcctg ngtgaaaatg gtattccgct tcacaatttc
                                                                       540
ccac
                                                                       544
      <210> 258
      <211> 418
      <212> DNA
      <213> Homo sapien
      <400> 258
agcgtggtcg cggccgaggt ccacatcggc agggtcggag ccctggccgc catactcgaa
                                                                        60
ctggaatcca tcggtcatgc tctcgccgaa ccagacatgc ctcttgtcct tggggttctt
                                                                       120
getgatgtae cagttettet gggecaeact gggetgagtg gggtaeacge aggteteace
                                                                       180
agtctccatg ttgcagaaga ctttgatggc atccaggttg cagccttggt tggggtcaat
                                                                       240
ccagtactct ccactcttcc agtcagagtg gcacatcttg aggtcacggc aggtgcgggc
                                                                       300
ggggttettg eggetgeect etgggeteeg gatgtteteg atetgetgge teaagetett
                                                                       360
gaagggtggt gtccacctcg aggtcacggt cacgaaacct gcccgggcgg ccgctcga
                                                                       418
      <210> 259
      <211> 377
      <212> DNA
      <213> Homo sapien
```

```
<220>
      <221> misc_feature
      <222> (1)...(377)
      <223> n = A, T, C or G
      <400> 259
agegtggteg eggeegaggt caagaaceee geeggeacet geegtgaeet caagatgtge
                                                                      60
cactotgact ggaagagtgg agagtactgg attgaccoca accaaggotg caacotggat
                                                                     120
gccatcaaag tcttctgcaa catggagact ggtgagacct gcgtgtaccc cactcagcc
                                                                     180
agtgtggccc agaagaactg gtacatcagc aagaacccca aggacaagag gcatgtctgg
                                                                     240
ttcggcgaga gcatgaccga tggattccag ttcgagtatg gcggccaggg ctccgaccct
                                                                     300
qccgatgtgg acctgcccgn gccggnccgc tcgaaaagcc cnaatttcca gncacacttg
                                                                     360
gccggccgtt actactg
                                                                     377
      <210> 260
      <211> 332
      <212> DNA
      <213> Homo sapien
      <400> 260
tcgagcggcc gcccgggcag gtccacatcg gcagggtcgg agccctggcc gccatactcg
                                                                      60
aactggaatc catcggtcat gctctcgccg aaccagacat gcctcttgtc cttggggttc
                                                                     120
ttgctgatgt accagttctt ctgggccaca ctgggctgag tggggtacac gcaggtctca
                                                                     180
ccagtctcca tgttgcagaa gactttgatg gcatccaggt tgcagccttg gttggggtca
                                                                     240
atccagtact ctccactctt ccagtcagag tggcacatct tgaggtcacg gcaggtgcgg
                                                                     300
geggggttct tgacctegge egegaceaeg et
                                                                     332
      <210> 261
      <211> 94
      <212> DNA
      <213> Homo sapien
      <400> 261
60
ttttttttt tttttttt tttttttt tttttttt
                                                                      94
      <210> 262
      <211> 650
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(650)
      <223> n = A, T, C or G
      <400> 262
agegtggteg eggeegaggt etggeattee ttegaettet etceageega getteecaga
                                                                     60
acatcacata tcactgcaaa aatagcattg catacatgga tcaggccagt ggaaatgtaa
                                                                     120
agaaggccct gaagctgatg gggtcaaatg aaggtgaatt caaggctgaa ggaaatagca
                                                                    180
aattcaccta cacagttctg gaggatggtt gcacgaaaca cactggggaa tggagcaaaa
                                                                    240
cagtctttga atatcgaaca cgcaaggctg tgagactacc tattgtagat attgcaccct
                                                                     300
atgacattgg tggtcctgat caagaatttg gtgtggacgt tggccctgtt tgcttttat
                                                                     360
aaaccaaact ctatctgaaa tcccaacaaa aaaaatttaa ctccatatgt gntcctcttg
                                                                     420
ttctaatctt ggcaaccagt gcaagtgacc gacaaaattc cagttattta tttccaaaat
                                                                     480
```

```
gtttggaaac agtataattt gacaaagaaa aaaggatact tctctttttt_tggctggtcc
                                                                        540
accaaataca attcaaaagg ctttttggtt ttatttttt anccaattcc aatttcaaaa
                                                                        600
tqtctcaatg gngcttataa taaaataaac tttcaccctt nttttntgat
                                                                        650
      <210> 263
      <211> 573
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(573)
      <223> n = A,T,C or G
      <400> 263
agcgtggtcg cggccgaggt ctgggatgct cctgctgtca cagtgagata ttacaggatc
                                                                         60
acttacggag aaacaggagg aaatagccct gtccaggagt tcactgtgcc tgggagcaag
                                                                        120
tctacagcta ccatcagcgg ccttaaacct ggagttgatt ataccatcac tgtgtatgct
                                                                        180
gtcactggcc gtggagacag ccccgcaagc agcaagccaa tttccattaa ttaccgaaca
                                                                        240
gaaattgaca aaccatccca gatgcaagtg accgatgttc aggacaacag cattagtgtc
                                                                        300
aagtggctgc cttcaagttc ccctgttact ggttacagaa gtaaccacca ctcccaaaaa
                                                                        360
tggaccagga ccaacaaaaa ctaaaactgc aggtccagat caaacagaaa atggactatt
                                                                       420
gaaggettge ageceaeagt ggaagtatgt ggntaggngt etatgeteag aateceaage
                                                                        480
eggagaaagt cageettetg gtttagactg cagtaaccaa cattgatege eetaaaggae
                                                                       540
tggncattca cttggatggt ggatgtccaa ttc
                                                                        573
      <210> 264
      <211> 550
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(550)
      <223> n = A, T, C or G
      <400> 264
tegageggee geeegggeag gteettgeag etetgeagng tettetteae cateaggtge
                                                                        60
agggaatage teatggatte cateeteagg getegagtag gteaccetgt acetggaaac
                                                                       120
ttgcccctgt gggctttccc aagcaatttt gatggaatcg acatccacat cagngaatgc
                                                                       180
cagtccttta gggcgatcaa tgttggttac tgcagtctga accagaggct gactctctcc
                                                                       240
gcttggattc tgagcataga cactaaccac atactccact gtgggctgca agccttcaat
                                                                       300
agtcatttct gtttgatctg gacctgcagt tttaagtttt tggtggtcct gncccatttt
                                                                       360
tgggaagtgg ggggttactc tgtaaccagt aacaggggaa cttgaaggca gccacttgac
                                                                       420
actaatgctg ttgtcctgaa catcggtcac ttgcatctgg ggatggtttt gacaatttct
                                                                       480
ggttcggcaa attaatggaa attggcttgc tgcttggcgg ggctgnctcc acgggccagt
                                                                       540
gacagcatac
                                                                       550
      <210> 265
      <211> 596
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
```

```
<222> (1)...(596)
       <223> n = A, T, C or G
       <400> 265
 tcgagcggcc gcccgggcag gtccttgcag ctctgcagtg tcttcttcac catcaggtgc
                                                                         60
 agggaatage teatggatte cateeteagg getegagtag gteaceetgt acetggaaae
                                                                        120
 ttgcccctgt gggctttccc aagcaatttt gatggaatcg acatccacat cagtgaatgc
                                                                        180
cagteettta gggegateaa tgttggttae tgcagtetga accagagget gaetetetee
                                                                        240
 gcttggattc tgagcataga cactaaccac atactccact gtgggctgca agccttcaat
                                                                        300
 agtcatttct gtttgatctg gacctgcagt tttaagtttt tgttggncct gnnccatttt
                                                                        360
tggggaaggg gtggttactc ttgtaaccag taacagggga acttgaagca gccacttgac
                                                                        420
 actaatgctg gtggcctgaa catcggtcac ttgcatctgg gatggtttgg tcaatttctg
                                                                        480
 ttcggtaatt aatgggaaat tggcttactg gcttgcgggg gctgtctcca cggncagtga
                                                                        540
 caagcataca caggngatgg gtataatcaa ctccaggttt aaggccnctg atggta
                                                                        596
       <210> 266
      <211> 506
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(506)
      <223> n = A, T, C or G
      <400> 266
agegtggteg eggeegaggt etgggatget eetgetgtea eagtgagata ttacaggate
                                                                        60
acttacggag aaacaggagg aaatagccct gtccaggagt tcactgtgcc tgggagcaag
                                                                        120
tctacagcta ccatcagcgg ccttaaacct ggagttgatt ataccatcac tgtgtatgct
                                                                       180
gtcactggcc gtggagacag ccccgcaagc agtaagccaa tttccattaa ttaccgaaca
                                                                        240
gaaattgaca aaccatccca gatgcaagtg accgatgttc aggacaacag cattagtgtc
                                                                        300
aagtggctgc cttcaagttc ccctgttact ggttacagag taaccaccac tcccaaaaat
                                                                        360
gggaccagga ccaacaaaaa actaaaactg canggtccag atcaaacaga aatgactatt
                                                                        420
gaaggettge ageceaeagt ggagtatgtg ggttagtgte tatgeteaga atnecaageg
                                                                        480
gagagagtca gcctctggtt cagact
                                                                        506
      <210> 267
      <211> 548
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(548)
      <223> n = A, T, C or G
      <400> 267
tegageggee geeegggeag gteagegete teaggaegte accaecatgg cetgggetet
                                                                        60
getectecte accetectea eteagggeae agggteetgg geceagtetg eeetgaetea
                                                                       120
gesteestee gegteegggt steetggasa gteagteass atsteetgsa etggaassag
                                                                       180
cagtgacgtt ggtgcttatg aatttgtctc ctggtaccaa caacacccag gcaaggcccc
                                                                       240
caaactcatg atttctgagg tcactaagcg gccctcaggg gtccctgatc gcttctctgg
                                                                       300
ctccaagtct ggcaacacgg cctccctgac cgtctctggg ctccangctg aggatgangc
                                                                       360
tgattattac tggaagctca tatgcaggca acaacaattg ggtgttcggc ggaagggacc
                                                                       420
aagctgaccg tnctaaggtc aagcccaagg cttgccccc tcggtcactc tgttcccacc
                                                                       480
  J.
```

```
ctcctctgaa gaagctttca agccaacaan gncacactgg gtgtgtctca taagtggact
                                                                        540 -
                                                                        548
      <210> 268
      <211> 584
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(584)
      <223> n = A, T, C or G
   ._ <400> 268
aqcgtggtcg cggccgaggt ctgtagcttc tgtgggactt ccactgctca ggcgtcaggc
                                                                         60
tcaggtagct gctggccgcg tacttgttgt tgctttgntt ggagggtgtg gtggtctcca
                                                                        120
etecegeett gaeggggetg etatetgeet tecaggeeae tgteaegget eeegggtaga
                                                                        180
agtcacttat gagacacacc agtgtggcct tgttggcttg aagctcctca gaggagggtg
                                                                        240
ggaacagagt gaccgagggg gcagcettgg gctgacctag gacggtcage ttggtccete
                                                                        300
egeogaacae ceaattgttg ttgeetgeat atgagetgea gtaataatea geeteateet .
                                                                        360
cageetggag eccagagaen gteaagggag geeegtgttt geeaagaett ggaageeaga
                                                                        420
naagegatea gggaceeetg agggeegett tacngacete aaaaaateat gaatttgggg
                                                                        480
ggcctttgcc tgggngttgg ttggtnacca gnaaaacaaa atttcataaa gcaccaacgt
                                                                        540
cactgctggt ttccagtgca ngaanatggt gaactgaant qtcc
                                                                        584
      <210> 269
      <211> 368
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(368)
      <223> n = A, T, C or G
      <400> 269
agegtggteg eggeegaggt ceageateag gageeeegee ttgeeggete tggteatege
                                                                         60
ctttcttttt gtggcctgaa acgatgtcat caattcgcag tagcagaact gccgtctcca
                                                                       120
ctgctgtctt ataagtctgc agcttcacag ccaatggctc ccatatgccc agttccttca
                                                                        180
tgtccaccaa agtacccgtc tcaccattta caccccaggt ctcacagttc tcctgggtgt
                                                                        240
gcttggcccg aagggaggta agtanacgga tggtgctggt cccacagttc tggatcaggg
                                                                       300
tacgaggaat gacctctagg gcctgggcna caagccctgt atggacctgc ccgggcgggc
                                                                        360
ccgctcga
                                                                        368
      <210> 270
      <211> 368
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(368)
      <223> n = A, T, C or G
      <400> 270
```

```
tegageggee geeegggeag gteeatacag ggetgttgee caggeeetag aggneattee
                                                                          60
 ttgtaccctg atccagaact gtgggaccag caccatccgt ctacttacct cccttcgggc
                                                                         120
 caagcacacc caggagaact gtgagacctg gggtgtaaat ggngagacgg gtactttggt
                                                                         180
 ggacatgaag gaactgggca tatgggagcc attggctgng aagctgcana cttataagac
                                                                         240
 agcagtggag acggcagttc tgctactgcg aattgatgac atcgtttcag gccacaaaaa
                                                                         300
 gaaaggcgat gaccanagcc ggcaaggcgg ggcttcctga tgctggacct cggccgccga
                                                                         360
 ccacqctt
                                                                         368
       <210> 271
       <211> 424
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(424)
      <223> n = A, T, C or G
       <400> 271
agegtggteg eggeegaggt ceaetagagg tetgtgtgee attgeecagg eagagtetet
                                                                         60
gcgttacaaa ctcctaggag ggcttgctgt gcggagggcc tgctatggtg tgctgcggtt
                                                                        120
catcatggag agtggggcca aaggctgcga ggttgtggtg tctggggaaac tccgaggaca
                                                                        180
gagggetaaa teeatgaagt ttgtggatgg eetgatgate cacageggag accetgttaa
                                                                        240
ctactacgtt gacactgctg tgcgccacgt gttgctcana cagggtgtgc tgggcatcaa
                                                                        300
ggtgaagatc atgctgccct gggacccanc tggcaaaaat ggcccttaaa aaccccttgc
                                                                        360
cntgaccacg tgaaccattt gtgngaaccc caagatgaan atacttgccc accaccccc
                                                                        420
attc
                                                                        424
      <210> 272
      <211> 541
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(541)
      <223> n = A, T, C or G
      <400> 272
tegageggee geeegggeag gtetgeeaag gagaeeetgt tatgetgtgg ggaetggetg
                                                                         60
gggcatggca ggcggctctg gcttcccacc cttctgttct gagatggggg tggtgggcag
                                                                        120
tatctcatct ttgggttcca caatgctcac gtggtcaggc aggggcttct tagggccaat
                                                                        180
cttaccagtt gggtcccagg gcagcatgat cttcaccttg atgcccagca caccctgtct
                                                                        240
gagcaacacg tggcgcacag cagtgtcaac gtagtagtta acagggtctc cgctgtggat
                                                                        300
catcaggcca tccacaaact tcatggattt agccctctgt cctcggagtt tcccaaaaca
                                                                        360
ccacaacctc gccagccttt gggccccact tcttcatgaa tgaaaccgca gcacaccatt
                                                                        420
ancaaggccc ttccgcacag gnaagccctt cctaaggagt tttgtaaacg caaaaaactc
                                                                        480
ttgcctgggg caaatgggca cacagacctn tantnggacc ttggnccgcg aaccaccgct
                                                                        540
                                                                        541
      <210> 273
      <211> 579
      <212> DNA
      <213> Homo sapien
```

```
<220>
      <221> misc feature
      <222> (1)...(579)
      <223> n = A, T, C or G
      <400> 273
agegtggteg eggeegaggt etggeeetee tggeaagget ggtgaagatg gteaccetgg
                                                                         60
aaaacccgga cgacctggtg agagaggagt tgttggacca cagggtgctc gtggtttccc
                                                                        120
tggaactcct ggacttcctg gcttcaaagg cattagggga cacaatggtc tggatggatt
                                                                        180
gaagggacag cccggtgctc ctggtgtgaa gggtgaacct ggngcccctg gtgaaaatgg
                                                                        240
aactccaggt caaacaggag cccgngggct tcctggngag agaggacgtg ttggtgccc
                                                                        300
tggcccanac ctgcccgggc ggccgctcna aaagccgaaa tccagnacac tggcggccgn
                                                                        360
tactantgga atccgaactt cggtaccaaa gcttggccgt aatcatggcc atagcttgtt
                                                                        420
ccctggggng gaaattggta ttccgctncc aattccacac aacataccga acccggaaag
                                                                        480
cattaaagtg taaaagccct gggggggcct aaatgangtg agcntaactc ncatttaatt
                                                                        540
ggcgttgcgc ttcactgccc cgcttttcca gtccgggna
                                                                        579
      <210> 274
      <211> 330
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(330)
      <223> n = A, T, C or G
      <400> 274
togagoggco gooogggcag gtotgggcca ggggcaccaa cacgtoctot otcaccagga
                                                                         60
agcccacggg ctcctgtttg acctggagtt ccattttcac caggggcacc aggttcaccc
                                                                        120
ttcacaccag gagcaccggg ctgtcccttc aatccatcca gaccattqtq ncccctaatq
                                                                        180
cctttgaagc caggaagtcc aggagttcca gggaaaccac gagcaccctg tggtccaaca
                                                                        240
actectetet caccaggteg teegggtttt ceagggtgae catetteace ageettgeea
                                                                        300
ggagggccag acctcggccg cgaccacgct
                                                                        330
      <210> 275
      <211> 97
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(97)
      <223> n = A, T, C or G
      <400> 275
ancgtggtcg cggccgaggt cctcaccaga ggtgncacct acaacatcat agtggaggca
                                                                         60
ctgaaagacc ancagaggca taaggttcgg gaagagg
                                                                         97
      <210> 276
      <211> 610
      <212> DNA
      <213> Homo sapien
      <220>
```

```
<221> misc_feature
   <222> (1)...(610)
      <223> n = A, T, C or G
      <400> 276
tegageggee geeegggeag gtecatttte teeetgaegg teceaettet etecaatett
                                                                         60
gtagttcaca ccattgtcat ggcaccatct agatgaatca catctgaaat gaccacttcc
                                                                        120
aaagcctaag cactggcaca acagtttaaa gcctgattca gacattcgtt cccactcatc
                                                                        180
tccaacggca taatgggaaa ctgtgtaggg gtcaaagcac gagtcatccg taggttggtt
                                                                        240
caageetteg ttgacagagt tgtecaeggt aacaacetet teeegaacet tatgeetetg
                                                                        300
ctqqtctttc aqtqcctcca ctatqatqtt qtaqqtqqca cctctqqtqa qqacctcnqn
                                                                        360
congaacaac gottaagooc gnattotgca gaataatooc atcacacttg goggoogott
                                                                        420
cgancatgca tentaaaagg ggccccaatt teeceettat aagngaance gtatttneca
                                                                        480
atttcactgg necegecgnt tttacaaacg neggtgaact ggggaaaaac eetggeggtt
                                                                        540
acccaacttt aatcgccntt ggcagcacaa tccccccttt tcgnccancn tgggcgtaaa
                                                                        600
taaccgaaaa
                                                                        610
      <210> 277
      <211> 38
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(38)
      <223> n = A, T, C or G
      <400> 277
ancgnggtcg cggccgangt ntttttttt ntttttt
                                                                         38
      <210> 278
      <211> 443
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(443)
      <223> n = A, T, C or G
      <400> 278
agcgtggtcg cggccgaggt ctgaggttac atgcgtggtg gtggacgtga gccacgaaga
                                                                        60
ccctgaggtc aagttcaact ggtacgtgga cggcgtggag gtgcataatg ccaagacaaa
                                                                       120
gccgcgggag gagcagtaca acagcacgta ccgggnggtc agcgtcctca ccgtcctgca
                                                                       180
ccagaattgg ttgaatggca aggagtacaa gngcaaggtt tccaacaaag ccntcccagc
                                                                       240
ccccntcgaa aaaaccattt ccaaagccaa agggcagccc cgagaaccac aggtgtacac
                                                                        300
cetgececca teeegggagg aaaagancaa naacenggtt cageettaae ttgettggte
                                                                        360
naangetttt tateecaaeg nactteecee ntggaantgg gaaaaaccaa tgggecaane
                                                                       420
cgaaaaacaa ttacaanaac ccc
                                                                        443
      <210> 279
      <211> 348
      <212> DNA
      <213> Homo sapien
```

```
<220>
      <221> misc_feature
      <222> (1)...(348)
      <223> n = A, T, C or G
      <400> 279
tegageggee geeegggeag gtgteggagt ceageaeggg aggegtggte ttgtagttgt
                                                                         60
teteeggetg eccattgete teceaeteea eggegatgte getgggatag aageetttga
                                                                       120
ccaggcaggt caggctgacc tggttcttgg tcatctcctc ccgggatggg ggcagggtga
                                                                       180
acacctgggg ttctcggggc ttgccctttg gttttgaana tggttttctc gatgggggct
                                                                       240
ggaagggett tgttgnaaac ettgeaettg acteettgee atteacceag neetggngea
                                                                       300
ggacggngag gacnetnace acaeggaace gggetggtgg actgetee
                                                                       348
      <210> 280
      <211> 149
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(149)
      <223> n = A, T, C or G
      <400> 280
agcgtggtcg cggacgangt cctgtcagag tggnactggt agaagttcca ngaaccctga
                                                                        60
actgtaaggg ttcttcatca gtgccaacag gatgacatga aatgatgtac tcagaagngn
                                                                       120
cctggaatgg ggcccatgan atggttgcc
                                                                       149
      <210> 281
      <211> 404
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(404)
      <223> n = A, T, C or G
      <400> 281
tegageggee geeegggeag gtecaceaea eccaatteet tgetggtate atggeageeg
                                                                        60
ccacgtgcca ggattaccgg ctacatcatc aagtatgaga agcctgggtc tcctcccaga
                                                                       120
gaagtggtcc ctcggccccg ccctggtgtc acagaggcta ctattactgg cctggaaccg
                                                                       180
ggaaccgaat atacaattta tgtcattgcc ctgaagaata atcagaagag cgagccctg
                                                                       240
attggaagga aaaagacaga cgagcttccc caactggtaa cccttccaca ccccaatctt
                                                                       300
catggaccag agatettgga tgtteettee acagtteaaa agaeeeettt eggeaeeeee
                                                                       360
cctgggtatg aacctgggaa aanggnantt aancttteet ggea
                                                                       404
      <210> 282
      <211> 507
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(507)
```

```
<223> n = A, T, C or G
      <400> 282
agegtggteg eggeegaggt etgggatget eetgetgtea eagtgagata ttacaggate
                                                                         60
acttacggag aaacaggagg aaatagccct gtccaggagt tcactgtgcc tgggagcaag
                                                                        120
tetacageta ceateagegg cettaaacet ggagttgatt ataccateae tgtgtatget
                                                                        180
gtcactggcc gtggagacag ccccgcaagc agcaagccaa tttccattaa ttaccgaaca
                                                                        240
qaaattgaca aaccatccca gatgcaagtg accgatgttc aggacaacag cattagtgtc
                                                                        300
aagtggctgc cttcaaggtn ccctggtact gggttacaga ntaaccacca ctcccaaaaa
                                                                        360
tqqaccaqga accacaaaaa cttaaactgc agggtccaga tcaaaacaga aatgactatt
                                                                        420
quangettge ageceacagt gggagtatgn gggtagtgne tatgetteag aatecaageg
                                                                        480
gaaaaangtc aagccttntq qqttcaa
                                                                        507
    - <210> 283
      <211> 325
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(325)
      <223> n = A, T, C or G
      <400> 283
tegageggee geeegggeag gteettgeag etetgeagtg tettetteac cateaggtge
                                                                         60<sup>©</sup>
agggaatage teatggatte cateeteagg getegagtag gteaccetgt acctggaaac
                                                                        120
ttgcccctgt gggctttccc aagcaatttt gatggaatcg acatccacat cagtgaatgc
                                                                        180
caqteettta gggegateaa tgttggttae tgcagnetga accagagget gaetetetee
                                                                        240
gettggatte tgageataga caetaaceae ataeteeaet gtgggetgea ancetteaat
                                                                        300
aanncatttc tgtttgatct ggacc
                                                                        325
      <210> 284
      <211> 331
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(331)
      <223> n = A, T, C or G
      <400> 284
tcgagcggcc gcccgggcag gtctggtggg gtcctggcac acgcacatgg gggngttgnt
                                                                         60
ctnatccage tgcccagece ccattggcga gtttgagaag gtgtgcagea atgacaacaa
                                                                        120
naccttcgac tcttcctgcc acttctttgc cacaaagtgc accctggagg gcaccaagaa
                                                                        180
qqqccacaag ctccacctgg actacatcgg gccttgcaaa tacatccccc cttgcctgga
                                                                        240
ctctgagetg accgaattcc cccttgcgca tgcgggactg gctcaagaac cgtcctggca
                                                                        300
cccttgtatg anagggatga agacacnacc c
                                                                        331
      <210> 285
      <211> 509
      <212> DNA
      <213> Homo sapien
      <220>
```

```
<221> misc feature
      <222> (1)...(509)
      <223> n = A,T,C or G
      <400> 285
agegtggteg eggeegaggt etgteetaea gteeteagga etetaeteee teageagegt
                                                                        60
ggtgaccgtg ccctccagca acttcggcac ccagacctac acctgcaacg tagatcacaa
                                                                       120
gcccagcaac accaaggtgg acaagagagt tgagcccaaa tcttgtgaca aaactcacac
                                                                       180
atgcccaccg tgcccagcac ctgaactcct ggggggaccg tcagtcttcc tcttcccccg
                                                                       240
catececett ccaaacetge eegggeggee getegaaage egaatteeag cacaetggeg
                                                                       300
gccggtacta gtggancena acttggnane caacetggng gaantaatgg gcataanetg
                                                                       360
tttctggggg gaaattggta tccngtttac aattcccnca caacatacga gccggaagca
                                                                       420
taaaagngta aaagcctggg ggnggcctan tgaagtgaag ctaaactcac attaattngc
                                                                       480
gttgccgctc actggcccgc ttttccage
                                                                       509
      <210> 286
      <211> 336
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(336)
      <223> n = A, T, C or G
      <400> 286
tcgagcggcc gcccgggcag gtttggaagg gggatgcggg ggaagaggaa gactgacggt
                                                                       - 60
cccccagga gttcaggtgc tgggcacggt gggcatgtgt gagttttgtc acaagatttg
                                                                       120
ggctcaactc tcttgtccac cttggtgttg ctgggcttgt gatctacgtt gcaggtgtag
                                                                       180
gtctgggngc cgaagttgct ggagggcacg gtcaccacgc tgctgaggga gtagagtcct
                                                                       240
gaggactgta ngacagacct cggccgngac cacgctaagc cgaattctgc agatatccat
                                                                       300
cacactggcg gccgctccga gcatgcattt tagagg
                                                                       336
      <210> 287
      <211> 30
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(30)
      <223> n = A, T, C or G
   <400> 287
agcgtggncg cggacganga caacaaccc
                                                                        30
      <210> 288
      <211> 316
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(316)
      <223> n = A, T, C or G
```

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```
<400> 288
tegageggee geeegggeag gneeacateg geagggtegg ageeetggee geeatacteg
                                                                         60
aactggaatc catcggtcat getettgeeg aaccagacat geetettgte ettggggtte
                                                                        120
ttgctgatgn accagttctt ctgggccaca ctgggctgag tggggtacac gcaggtctca
                                                                        180
ccagteteca tgttgcagaa gaetttgatg gcatecaggt tgcageettg gttggggtca
                                                                        240
atccagtact ctccactctt ccagtcagag tggcacatct tgaggtcacg gcaggtgcgg
                                                                        300
gcggggttct tgacct
                                                                        316
      <210> 289
      <211> 308
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(308)
      <223> n = A, T, C or G
      <400> 289
agcgtggtcg cggccgaggt ccagcctgga gataanggtg aaggtggtgc ccccqgactt
                                                                         60
ccaggtatag ctggacctcg tggtagccct ggtgagagag gtgaaactgg ccctccagga
                                                                        120
cctgctggtt tccctggtgc tcctggacag aatggtgaac ctggnggtaa aggagaaaga
                                                                        180
qqqqctccgg ntganaaagg tgaaggaggc cctcctgnat tggcaggggc cccangactt
                                                                        240
agaggtggag ctggcccccc tggccccgaa ggaggaaagg gtgctgctgg tcctcctggg
                                                                        300
ccacctgg
                                                                        308
      <210> 290
      <211> 324
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(324)
      <223> n = A, T, C or G
      <400> 290
togagoggco gocogggcag gtotgggcoa ggaggaccaa taggaccagt aggacccctt
                                                                         60
gggccatctt tccctgggac accatcagca cctggaccqc ctqqttcacc cttgtcaccc
                                                                        120
tttggaccag gacttccaag acctcctctt tctccaggca ttccttgcag accaggagta
                                                                        180
ccancagcac caggtggccc aggaggacca gcagcaccct ttcctccttc gggaccaggg
                                                                        240
ggaccagete cacetetaag teetggggee eetgecaate caggagggee teetteacet
                                                                        300
ttctcacccg gagcccctct ttct
                                                                        324
      <210> 291
      <211> 278
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(278)
      <223> n = A, T, C or G
```

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<400> 291
tegageggee geeegggeag gtecaeeggg atattegggg gtetggeagg aatgggagge
                                                                                                                                                                          60 -
atccagaacg agaaggagac catgcaaagc ctgaacgacc gcctqqcctc ttacctqqac
                                                                                                                                                                       120
agagtgagga gcctggagac cgacaaccgg aggctggaga gcaaaatccg qqaqcacttq
                                                                                                                                                                       180
gagaagaagg gaccccaggt cagagactgg agccattact tcaagatcat cgaggacctg
                                                                                                                                                                       240
agggeteana tettegeaaa taetgengae aatgeeeg
                                                                                                                                                                       278
              <210> 292
              <211> 299
              <212> DNA
              <213> Homo sapien
              <220>
              <221> misc feature
              <222> (1)...(299)
              <223> n = A, T, C or G
              <400> 292
atgcgnggtc gcggccgang accanctctg gctcatactt gactctaaag ncntcaccag
                                                                                                                                                                          60
nanttacggn cattgccaat ctgcagaacg atgcgggcat tgtccgcant atttgcgaag
                                                                                                                                                                        120
atctgagccc tcaggncctc gatgatcttg aagtaanggc tccagtctct gacctggggt
                                                                                                                                                                        180
contents can be a considered and the content of the
                                                                                                                                                                        240
netteteaet etgteeagga aaagaggeea ggeggnegat eagggetttt geatggaet
                                                                                                                                                                        299
               <210> 293
               <211> 101
               <212> DNA
               <213> Homo sapien
               <400> 293
agcgtggtcg cggccgaggt tgtacaagct ttttttttt tttttttt tttttttt
                                                                                                                                                                           60
tttttttt ttttttt ttttttt ttttttt t
                                                                                                                                                                        101
               <210> 294
               <211> 285
               <212> DNA
               <213> Homo sapien
               <220>
               <221> misc feature
               <222> (1)...(285)
               <223> n = A, T, C or G
               <400> 294
 tegageggee geeegggeag gtetgeeaac accaagattg geeeeggeeg catecacaca
                                                                                                                                                                           60
 gttngtgtgc ggggaggtaa caagaaatac cgtgccctga ggntggacgn ggggaatttc
                                                                                                                                                                        120
 tcctggggct cagagtgttg tactcgtaaa acaaggatca tcgatgttgt ctacaatgca
                                                                                                                                                                        180
 totaataacq agotqqttcq taccaaqacc ctqqtqaaqa attqcatcqt qctcatnqac
                                                                                                                                                                        240
 agcacaccgt accgacagtg ggtaccgaag teccaetatg enect
                                                                                                                                                                        285
               <210> 295
               <211> 216
               <212> DNA
```

<213> Homo sapien

```
<400> 295
tcgagcggcc gcccgggcag gtccaccaca cccaattcct tgctggtatc atggcagccg
                                                                         60
ccacgtgcca ggattaccgg ctacatcatc aagtatgaga agcctgggtc tcctcccaga
                                                                        120
gaagtggtcc ctcggccccg ccctggtgtc acagaggcta ctattactqq cctqqaaccq
                                                                        180
ggaaccgaat atacaattta tgtcattgcc ctgaag
                                                                        216
      <210> 296
      <211> 414
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(414)
    (223) n = A, T, C \text{ or } G
      <400> 296
agcgtgntcn cggccgagga tggggaagct cgnctgtctt tttccttcca atcaggggct
                                                                        60
nnntcttctg attattcttc agggcaanga cataaattgt atattcggnt cccggttcca
                                                                        120
gnccagtaat agtagcctct gtgacaccag ggcggggccg agggaccact tctctgggag
                                                                       180
gagacccagg cttctcatac ttgatgatga agccggtaat cctggcacgt gggcggctgc
                                                                       240
catgatacca ccaangaatt gggtgtggtg gacctgcccg ggcqqqccqc tcqaaaancc
                                                                       300
gaattentge aagaatatee ateacacttg ggegggeegn tegaaceatg catentaaaa
                                                                       360
gggccccaat ttccccccta ttaggngaag ccncatttaa caaattccac ttgg
                                                                        414
      <210> 297
      <211> 376
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(376)
      <223> n = A, T, C or G
      <400> 297
togagoggeo geoogggeag gtotogoggt ogcactogtq atqctqqtcc tqttqqtccc
                                                                        60
cccggccctc ctggacctcc tggtccccct ggtcctccca gcgctggttt cgacttcagc
                                                                       120
ttcctgcccc agccacctca agagaaggct cacgatggtg gccgctacta ccgggctgat
                                                                       180
gatgccaatg tggttcgtga ccgtgacctc gaggtggaca ccaccctcaa gagccttgag
                                                                       240
ccaqcaqaat cqaaaacatt cqqaacccaa qaaqqqcaaq cccqcaaaqa aaccccqccc
                                                                       300
gcacctggcc gngaacctcc aagaangtgc ccacntcttg actgggaaaa aaagggaaaa
                                                                       360
ntacttggaa ttggac
                                                                       376
     <210> 298
      <211> 357
      <212> DNA
      <213> Homo sapien
     <220>
     <221> misc feature
      <222> (1)...(357)
      <223> n = A, T, C or G
      <400> 298
```

3

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agogtggtog oggoogaggt coacatoggo agggtoggag cootggoogo catactogaa
                                                                        60
ctggaatcca tcggtcatgc tctcgccgaa ccagacatgc ctcttgtcct tggggttctt
                                                                       120
gctgatgtac cagttettet gggccacact gggctgagtg gggtacacgc aggtetcacc
                                                                       180
agtetecatg ttgcagaaga etttgatgge atccaggttg cageettggt tggggtcaat
                                                                       240
ccagtactet ccactettee agteagaagt ggeacatett gaggteaegg eagggtgegg
                                                                       300
gcggggttct tgcgggctgc ccttctgggc tcccggaatg ttctnngaac ttgctqq
                                                                       357
      <210> 299
      <211> 307
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(307)
      <223> n = A, T, C or G
      <400> 299
agogtggtog oggocgaggt coactagagg totgtgtgco attgcccagg cagagtotot
                                                                        60
gcgttacaaa ctcctaggag ggcttgctgt gcggagggcc tgctatggtg tgctgcggtt
                                                                       120
catcatqqaq agtggggcca aaggctgcga ggttgtggtg tctgggaaac tccgaggaca
                                                                       180
gagggctaaa tccatgaagt ttgtggatgg cctgatgatc cacagcggag accctgttaa
                                                                       240
                                                                       300
ctactacgtt gacacttgct tgtgcgccac gtgttgctca nacangggtg ggctgggcat
                                                                       307
caaggng
      <210> 300
      <211> 351
      <212> DNA
      <213> Homo sapien
      <400> 300
togagoggco gooogggcag gtotgccaag gagacoctgt tatgctgtgg ggactggctg
                                                                        60
qqqcatqqca qqcqqctctg gcttcccacc cttctgttct gagatggggg tggtgggcag
                                                                       120
                                                                       180
tatctcatct ttqqqttcca caatgctcac gtggtcaggc aggggcttct tagggccaat
cttaccagtt gggtcccagg gcagcatgat cttcaccttg atgcccagca caccetgtct
                                                                       240
                                                                       300
gagcaacacg tggcgcacag caagtgtcaa cgtaagtaag ttaacagggt ctccgctgtg
                                                                       351
qatcatcagg ccatccacaa acttcatgga tttaaccctc tgtcctcgga g
      <210> 301
      <211> 330
      <212> DNA
      <213> Homo sapien
      <400> 301
                                                                         60
tegageggee geeegggeag gtgttteaga ggtteeaagg tecaetgtgg aggteeeagg
agtgctggtg gtgggcacag aggtccgatg ggtgaaacca ttgacataga gactgttcct
                                                                        120
qtccaqqqtq taqqqqccca gctctttgat gccattggcc agttggctca gctcccagta
                                                                        180
cagccgctct ctgttgagtc cagggctttt ggggtcaaga tgatggatgc agatggcatc
                                                                        240
cactccagtg gctgctccat ccttctcgga cctgagagag gtcagtctgc agccagagta
                                                                        300
cagagggcca acactggtgt tctttgaata
                                                                        330
      <210> 302
      <211> 317
      <212> DNA
      <213> Homo sapien
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<220>
      <221> misc feature
      <222> (1)...(317)
      <223> n = A, T, C or G
      <400> 302
agcgtggtcg cggccgaggt ctgtactggg agctaagcaa actgaccaat gacattgaag
                                                                         60
agctgggccc ctacaccctg gacaggaaca gtctctatgt caatggtttc acccatcaga
                                                                        120
getetgtgne caccaccage actectggga cetecacagt ggattteaga aceteaggga
                                                                        180
ctccatcctc cctctccage cccacaatta tggctgctgg ccctctcctg gtaccattca
                                                                        240
ccctcaactt caccatcacc aacctgcagt atggggagga catgggtcac cctgnctcca
                                                                        300
ggaagttcaa caccaca
                                                                        317
      <210> 303
      <211> 283
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(283)
      <223> n = A, T, C \text{ or } G
      <400> 303
togagoggeo geoeggacag gtotgggegg atageacegg geatattttg gaatggatga
                                                                         60
ggtctggcac cctgagcagt ccagcgagga cttggtctta gttgagcaat ttggctagga
                                                                        120
ggatagtatg cagcacggnt ctgagnctgt gggatagctg ccatgaagta acctgaagga
                                                                        180
ggtgctggct ggtangggtt gattacaggg ttgggaacag ctcgtacact tgccattctc
                                                                        240
tgcatatact ggttagtgag gtgagcctgg ccctcttctt ttg
                                                                        283
      <210> 304
      <211> 72
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(72)
      <223> n = A, T, C or G
      <400> 304
agcgtggtcg cggccgaggt gagccacagg tgaccggggc tgaagctggg gctgctggnc
                                                                         60
ctgctggtcc tg
                                                                         72
      <210> 305
      <211> 245
      <212> DNA
      <213> Homo sapien
     <220>
     <221> misc feature
     <222> (1)...(245)
     <223> n = A, T, C or G
```

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```
<400> 305
cagengetee nacggggeet gngggaccaa caacacegtt tteaccetta ggeeetttgg
                                                                         60
ctcctctttc tcctttagca ccaggttgac cagcagence ancaggacca gcaaatccat
                                                                        120
tggggccagc aggaccgacc tcaccacgtt caccagggct tccccgagga ccagcaggac
                                                                        180
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agagtgagga gcctggagac cganaaccgg aggctggana gcaaaatccg ggagcacttg
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      <223> n = A, T, C or G
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ctgagecete aggteetega tgatettgaa gtaatggete cagtetetga eetggggtee
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cctcactctg tccaggtaag aaggcccagg cggtcgttca ggctttgcat ggtctccttc
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gatcagtcag actggctgtt ctcagttctc acctgagcaa ggtcagtctg cagccagagt
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acagagggcc aacactggtg ttcttgaaca agggcttgag cagaccctgc agaaccctct
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ttggtgatgg
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getgatgtae cagttettet gggeeacaet gggetgagtg gggtaeaceg eaggteteae
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cagtetecat gttgcagaag aetttgatgg catecaggtt geageettgg ttggggtcaa
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tccagtacte tecaetette cagteagaag tgggcacate ttgaggteae eggeaggtge
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cgggccgggg gttcttgcgg cttgccctct gggctccgga tgttctcgat ctgcttggct
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cccgctcga
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cgcacctgcc gtgacctcaa gatgtgccac tctgactgga agagtggaga gtactggatt
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                                                                       240
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                                                                       300
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                                                                      1500
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gatctgcaat gactggaact tgccggtgcc tggggtgcct ttcccccaqc caqqqtccaa
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<212> PRT

<213> Homo sapien

<400> 312

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 Leu
 Cys
 Pro
 Pro
 Leu
 Ala
 Phe

 Leu
 Gly
 Pro
 Pro
 Gln
 Trp
 Trp
 Glu
 His
 Leu
 Gly
 Leu
 Gln
 Phe
 Leu

 Asn
 Leu
 Pro
 Arg
 Leu
 Pro
 Ala
 Leu
 Ser
 Trp
 Cys
 Tyr
 Ser
 Leu
 Ser

 Thr
 Ser
 Pro
 Arg
 Met
 Arg
 Arg
 Thr
 Cys
 Ser
 Thr
 Leu

 Ala
 Pro
 Gly
 Met
 Arg
 Arg
 Thr
 Cys
 Ser
 Thr
 Leu
 Ser
 Fro
 Re
 Re

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		115					120					125	Asp	_	
	130					135					140		Thr		
145					150					155			Gly		160
				165					170	-			Pro	175	
			180					185					Pro 190		
.3		195					200					205	Ile		
	210					215					220		Phe		
225	•				230					235			Lys		240
				245					250				Leu	255	
			260					265					Thr 270		_
		275					280					285	Tyr		
	290					295					300		Tyr		
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				325					330				Thr	335	
			340					345					Gln 350		
		355					360					365	Leu		
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				405					410				Ile	415	
			420					425					430 Asn		
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	450					455					460		Gly		
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				485		,			490				Glu	495	
			500					505					510 Met	_	
		515					520					525	Lys		
			1	- 1 -					u	· · · · · · · · · · · · · · · · · · ·	0	U L U	Lys	vah	GTA

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535
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Ala-Ala Thr Gly Val Asp Thr Thr Cys Thr Tyr His Pro Asp Pro Val
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Gly Pro Gly Leu Asp Ile Gln Gln Leu Tyr Trp Glu Leu Ser Gln Leu
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Thr His Gly Val Thr Gln Leu Gly Phe Tyr Val Leu Asp Arg Asp Ser
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Leu Phe Ile Asn Gly Tyr Ala Pro Gln Asn Leu Ser Ile Arg Gly Glu
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Tyr Gln Ile Asn Phe His Ile Val Asn Trp Asn Leu Ser Asn Pro Asp
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Pro Thr Ser Ser Glu Tyr Ile Thr Leu Leu Arg Asp Ile Gln Asp Lys
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Val Thr Thr Leu Tyr Lys Gly Ser Gln Leu His Asp Thr Phe Arg Phe
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Cys Leu Val Thr Asn Leu Thr Met Asp Ser Val Leu Val Thr Val Lys
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Ala Leu Phe Ser Ser Asn Leu Asp Pro Ser Leu Val Glu Gln Val Phe
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Leu Asp Lys Thr Leu Asn Ala Ser Phe His Trp Leu Gly Ser Thr Tyr
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Gln Leu Val Asp Ile His Val Thr Glu Met Glu Ser Ser Val Tyr Gln
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                                        715
Pro Thr Ser Ser Ser Thr Gln His Phe Tyr Leu Asn Phe Thr Ile
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                                    730
Thr Asn Leu Pro Tyr Ser Gln Asp Lys Ala Gln Pro Gly Thr Thr Asn
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                                745
Tyr Gln Arg Asn Lys Arg Asn Ile Glu Asp Ala Leu Asn Gln Leu Phe
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                                               765
Arg Asn Ser Ser Ile Lys Ser Tyr Phe Ser Asp Cys Gln Val Ser Thr
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                                            780
Phe Arg Ser Val Pro Asn Arg His His Thr Gly Val Asp Ser Leu Cys
                    790
                                       795
Asn Phe Ser Pro Leu Ala Arg Arg Val Asp Arg Val Ala Ile Tyr Glu
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                                   810
Glu Phe Leu Arg Met Thr Arg Asn Gly Thr Gln Leu Gln Asn Phe Thr
           820
                                825
Leu Asp Arg Ser Ser Val Leu Val Asp Gly Tyr Phe Pro Asn Arg Asn
                            840
Glu Pro Leu Thr Gly Asn Ser Asp Leu Pro Phe Trp Ala Val Ile Leu
                        855
                                            860
Ile Gly Leu Ala Gly Leu Leu Gly Leu Ile Thr Cys Leu Ile Cys Gly
                    870
                                        875
Val Leu Val Thr Thr Arg Arg Arg Lys Lys Glu Gly Glu Tyr Asn Val
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<211> 656

<212> DNA

<213> Homo sapiens

× .

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<212> DNA
<213> Homo sapiens
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cagttatgtt taactgggct ctctgacacc gggaggaagg tggcggggtt taggtgttgc 240
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cattcattag ctaatggtgt cctttggtat ttattaaaat caccacagca tagggggact 360
ttatgtttag gttttgtcta agagttagct tatctgcttc ttgtgctaac agggctattq 420
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<212> DNA
<213> Homo sapiens
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 <212> DNA
 <213> Homo sapiens
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 <223> n = A, T, C or G
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<400> 320
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<213> Homo sapiens
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<212> DNA
<213> Homo sapiens
<400> 323
gggccctggg cgcttccaaa tgacccagga ggtggtctgc gacgaatgcc ctaatgtcaa 60
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<210> 324
<211> 354
<212> DNA
<213> Homo sapiens
<400> 324
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ageggtetgt atggaeccag gettgteaaa etgtaetata eacategtga eagteaccat 120
taacggagat gatgccgaaa acgcaaggcc gaagccaaag ccaggggatg gagagtttgt 180
ggaagtcatt totttaccca agaatgacct gctgcagaga cttgatgctc tggtagctga 240
agaacatete acagtggacg ccagggteta ttectaeget etagegetga aacatgcaaa 300
tgcaaagcca tttgaagtgc ccttcttgaa attttaagcc caaatatgac actg
<210>-325
<211> 642
<212> DNA
<213> Homo sapiens
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<222> (1)...(642)
<223> n = A, T, C \text{ or } G
<400> 325
ncatgettga atgggeteet ggtgagagat tgeeceetgg tggtgaaaca ategtgtgtg 60
cccactgata ccaagaccaa tgaaagagac acagttaagc agcaatccat ctcatttcca 120
ggcacticaa taggicgctg attggicctt gcaccagcag tggtagtcgt acctattca 180
gagaggtetg aaattcaggt tettagtttg ccagggacag geectacett atatttttt 240
ccatcttcat catccacttc tgcttacagt ttgctgctta caataactta atgatggatt 300
gagttatetg ggtggtetet agecatetgg geagtgtggt tetgtetaac eaaagggeat 360
tggcctcaaa ccctgcattt ggtttagggg ctaacagagc tcctcagata atcttcacac 420
 acatgtaact getggagate ttattetatt atgaataaga aacgagaagt ttttecaaag 480
 tgttagtcag gatctgaagg ctgtcattca gataacccag cttttccttt tggcttttag 540
 cccattcaga ctttgccaga gtcaagccaa ggattgcttt tttgctacag ttttctgcca 600
 aatggcctag ttcctgagta cctggaaacc agagagaaag ag
 <210> 326
 <211> 455
 <212> DNA
 <213> Homo sapiens
 <400> 326
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 accttcacct tetegetett ectgetettg teattgacaa acttecegta ecaggeattg 120
 acgatgatga ggcccattct ggactcttct gcctcaatta tccttcggac agattcctgc 180
 atcagecgga cageggacte egectettge ttettetgea geacateggt ggeggegett 240
 tecetetget tetecaatte ettetette tgageeetga ggtatggttt gatgateaga 300
 cggtgcatgg caaagtagac cactagaggc cccacggtgg catagaacat ggcgctgggc 360
 agaagctggt ccgtcaagtg aatagggaag aagtatgtct gactggccct gttgagcttg 420
                                                                    455
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 <210> 327
  <211> 321
  <212> DNA
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<213> Homo sapiens
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aagccaccct cttcccgcag catggtgaac aggaagttca taaggacggc gtgtttgcga 180
ggatatttct gacacagggc actgatggcc tggacaacca ccaccttgaa ttcatccgag 240
atttctgaca tgaaggagga gatctgcttc atgaggcggt cgatgctgct ctcgctgccc 300
qtcttaaqqa qqqtqqtqat q
<210> 328
<211> 476
<212> DNA
<213> Homo sapiens
<220> -
<221> misc feature
<222> (1)...(476)
<223> n = A, T, C or G
<400> 328
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cagtgtgcag tctgatgaag tctgggtggg tgtggtctac gggctggcag ctaccatgat 120
ccaagaggta atgcactcct tttcccatct ctccaccatc tgtatcctgg ccmagaaaaa 180
cttcccttca aaccaaccaa aatttccttt caaaggcata acccaaatgc catccttggt 240
coggtotaat aaagcotoco coattitico octggtatgo attoccaggo tocctggoot 300
tncagggett netgtetgtg ggteatagtt tateteetee eacttgetgg gageteettg 360
aaggcaaaga ctctactgcc tccatctatc cagtggaagt ggctcttcag agggtgccaa 420
gttagtatgt atgactgtca teteteceaa cagggeetga ettggsaggg etteca
<210> 329
<211> 340
<212> DNA
<213> Homo sapiens
<400> 329
cgagggagat tgccagcacc ctgatggaga gtgagatgat ggagatcttg tcagtgctag 60
ctaagggtga ccacagccct gtcacaaggg ctgctgcagc ctgcctggac aaagcagtgg 120
aatatgggct tatccaaccc aaccaagatg gagagtgagg gggttgtccc tgggcccaag 180
gctcatgcac acgctaccta ttgtggcacg gagagtaagg acggaagcag ctttggctgg 240
tggtggctgg catgcccaat actcttgccc atcctcgctt gctgccctag gatgtcctct 300
gttctgagtc agcggccacg ttcagtcaca cagccctgct
                                                                   340
<210> 330
<211> 277
<212> DNA
<213> Homo sapiens
<400> 330
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caggatgcag ccagtgctga cattgttgag gtgcaggagc tctactccat taagggagaa 120
ggccaggcca aaaaggttgt tggcaatcca gtgcttcctc agcaggtacc agacgccaac 180
gatgctgctc aggcccaggc acaccaggtc cttggtgtca aattcataat tgatgatctc 240
ctccttgttt tcccagaacc ctgtgtgaag agcagac
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<210> 331
<211> 136
<212> DNA
<213> Homo sapiens
<400> 331
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atacaaacca cacacacaat gaggatgaaa acagataaca ggtaaaatga cctcacctgc 120
ccgggcggcc gctcga
<210> 332
<211> 184
<212> DNA
<213> Homo sapiens
<400> 332
ttgtgagata aacgcagata ctgcaatgca ttaaaacgct tgaaatactc atcagggatg 60
ttgctgatct tattgttgtc taagtagaga gttagaagag agacagggag accagaaggc 120
agtotggota totgattgaa gotcaagtoa aggtattoga gtgatttaag acotttaaaa 180
gcag
 <210> 333
 <211> 384
 <212> DNA
 <213> Homo sapiens
 <400> 333
 cggaaaactt cgaggaattg ctcaaagtgc tgggggtgaa tgtgatgctg aggaagattg 60
 ctgtggctgc agcgtccaag ccagcagtgg agatcaaaca ggagggagac actttctaca 120
 tcaaaacctc caccaccgtg cgcaccacag agattaactt caaggttggg gaggagtttg 180
 aggagcagac tgtggatggg aggccctgta agagcctggt gaaatgggag agtgagaata 240
 aaatggtetg tgagcagaag eteetgaagg gagagggeee caagaceteg tggaccagag 300
 aactgaccaa cgatggggaa ctgatcctga ccatgacggc ggatgacgtt gtgtgcacca 360
 gggtctacgt ccgagagtga gcgg
 <210> 334
 <211> 169
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(169)
 <223> n = A,T,C or G
  <400> 334
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  aaaattgaat ttccacttcc tgaccgccgc cagaagagat tgattttctc cactatcact 120
  agcaagatga acctctctga ggaggttgac ttggaagact atgtngccc
                                                                     169
  <210> 335
  <211> 185
  <212> DNA
  <213> Homo sapiens
```

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<400> 335
ccaggtttgc agcccaggct gcacatcagg ggactgcctc gcaatacttc atgctgttgc 60
tgctgactga tggtgctgtg acggatgtgg aagccacacg tgaggctgtg gtgcgtgcct 120
cgaacctgcc catgtcagtg atcattgtgg gtgtgggtgg tgctgacttt gaggccatgg 180
<210> 336
<211> 358
<212> DNA
<213> Homo sapiens
<220>
. <221> misc feature
<222> (1) ... (358)
<223> n = A, T, C or G
<400> 336
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tttgttctca gtcccatcca actccagcat caggttgtcc agtttctctt gctccaccac 120
agagagacet gagetgatga gggetggege gatggtggag ttgatgtggt ceaetgeett 180
caggacacct ttgcctaagt aacgctgttt gtctccatcc ctcagctcca gggcctcata 240
gatgcccgta gaggctccac tgggcactgc agcccggaaa agacctttgg cagtatagag 300
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<210> 337
<211> 271
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(271)
<223> n = A, T, C or G
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gaaateetge ccageatggg atteagaace tggtetgeaa ccaaateeae cgteaaagtt 120
catacaggat aaaacaaatt caattgcctt ttccacatta atagcatcaa gcttccccaa 180
caaagccaaa gttgccaccg cacaaaaaga gaatcttgtg tcaatttctc cctactttat 240
aaaagtagat ttttcacatc ccatgaagca g
<210> 338
<211> 326
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(326)
<223> n = A, T, C or G
<400> 338
ctgtgctccc gactngnnca tctcaggtac caccgactgc actgggcggg gccctctggg 60
gggaaaggct ccacggggca gggatacatc tcgaggccag tcatcctctg gaggcagccc 120
aatcaggtca aagattttgc ccaactggtc ggcttcagag tttccacaga agagaggctt 180
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tcgacgaaac atctctgcaa agatacagcc aacactccac atgtccacag gtgttgcata 240
tgtggactgc agaagaactt cgggagctcg gtaccagagt gtaacaacca cgggtgtaag 300
tgccatctgg tagctgtaga ttctgg
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<210> 339
<211> 260
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(260)
<223> n = A, T, C or G
<400> 339
ttcacctgag gactcatttc gtgccctttg ttgacttcaa gcaaagncct tcanggtctn 60
caaggacgnc acatttccac ttgcgaatgn nctcanggct catcttgaag aanaagnanc 120
ccaagtgctg gatcccagac tcgggggtaa ccttgtgggt aagagctcat ccagtttatg 180
ctttaggacg tecanetact egggggaget ggaageetge gtggatgegg eeetgetgga 240
cctcggccgc gaccacgcta
<210> 340
<211> 220
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(220)
<223> n = A, T, C or G
<400> 340
ctggaageee ggetnggnet ggeageggaa ggageeagge aggtteaege ageggtgetg 60
quagtagegg tageggeact egtetatgte caeacacteg ggeoegatet tgeggtaace 120
atcagggcag gtgcactgat aggagccagg caagttatgg cagtcctggc tggggcgaca 180
gtcgtgcagg gcctgggcac actcgtccac atccacacag
<210> 341
<211> 384
<212> DNA
<213> Homo sapiens
<400> 341
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gatggagett cacacgattt ceteetgegg cageggegaa ggteetetae tgetacaceg 120
ggcgtcacca gtggcccgtc tgcctcagga actcctccga gtgagggagg agggggctcc 180
tttcccagga tcaaggccac agggaggaag attgcacggg cactgttctg aggaggaagc 240
cccgttggct tacagaagtc atggtgttca taccagatgt gggtagccat cctgaatggt 300
qqcaattata tcacattgag acagaaattc agaaagggag ccaqccaccc tqqqqcaqtq 360
aagtgccact ggtttaccag acag
<210> 342
<211> 245
<212> DNA
<213> Homo sapiens
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tgtaaccaac aagaatgacc ccaagtccat caactetega gtetteattg gaaaceteaa 120
cacagetetg gtgaagaaat cagatgtgga gaccatette tetaagtatg geegtgtgge 180
eggetgttet gtgcacaagg getatgeett tgttcagtac tecaatgage gecatgeeeg 240
ggcag
<210> 343
<211> 611
<212> DNA
<213> Homo sapiens
<4.00> 343
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tttcctgcca gtgtcagaaa atcctattta tgaatcctgt cggtattcct tggtatctga 180
aaaaaatacc aaatagtacc atacatgagt tatttctaag tttgaaaaat aaaaagaaat 240
tgcatcacac taattacaaa atacaagtto tggaaaaaat attttctto attttaaaac 300
tttttttaac taataatggc tttgaaagaa gaggcttaat ttgggggtgg taactaaaat 360
caaaagaaat gattgacttg agggtctctg tttggtaaga atacatcatt agcttaaata 420
agcagcagaa ggttagtttt aattatgtag cttctgttaa tattaagtgt tttttgtctg 480
ttttacctca atttgaacag ataagtttgc ctgcatgctg gacatgcctc agaaccatga 540
atagcccgta ctagatcttg ggaacatgga tcttagagtc ctttggaata agttcttata 600
taaatacccc c
<210> 344
<211> 311
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(311)
<223> n = A, T, C or G
<400> 344
nctcgaaaaa gcccaagaca gcagaagcag acacctccag tgaactagca aagaaaagca 60
aagaagtatt cagaaaagag atgtcccagt tcatcgtcca gtgcctgaac ccttaccgga 120
aacctgactg caaagtggga agaattacca caactgaaga ctttaaacat ctggctcgca 180
agctgactca cggtgttatg aataaggagc tgaagtactg taagaatcct gaggacctgg 240
agtgcaatga gaatgtgaaa cacaaaacca aggantacat taanaagtac atgcannaan 300
tttggggctt g
<210> 345
<211> 201
<212> DNA
<213> Homo sapiens
<400> 345
cacacggtca tecegactge caacetggag geecaggeee tgtggaagga geegggeage 60
aatgtcacca tgagtgtgga tgctgagtgt gtgcccatgg tcagggacct tctcaggtac 120
ttctactccc gaaggattga catcaccctg tcgtcagtca agtgcttcca caagctggcc 180
tetgectatg gggccaggca g
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<210> 346
<211> 370
<212> DNA
<213> Homo sapiens
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cagaaaggac ttgagggaaa ggcgctggca gacggggtcg ctctccaqct tctccaaqac 180
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qttqqtqaca taaggcaggt agacccggcg gaagtctggg gcgtggttca ggactacgtc 300
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ggcgctgacg
<210> 347
<211> 416
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(416)
<223> n = A, T, C or G
<400> 347
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ccccatttga acaagcaaag aaggtgataa ccatgtttgt acagcgacag gtgtttgctg 120
aqaacaaqqa tqaqattgct ttagtcctgt ttggtacaga tggcactgac aatccccttt 180
ctggtgggga tcagtatcag aacatcacag tgcacagaca tctgatgcta ccagattttg 240
atttgctgga ggacattgaa agcaaaatcc aaccaggttc tcaacaggct gacttcctgg 300
atgcactaat cgtgagcatg gatgtgattc aacatgaaac aataggaaag aagtttggag 360
aagaggcata ttgaaatatt cactgacctc aagcagcccg attcagcaaa agtcan
<210> 348
<211> 351
<212> DNA
<213> Homo sapiens
<400> 348
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cagttggatg ctctcctgga ggctctgaaa ttgaaacggg caggaaatag tctggcagcc 120
tctacaqcaq aaqaaacqqc aggcaqtqcc caggqacqaq caqqaqacaq atqccttcct 180
cttqtctcaa ctgcaaagag gcgttccttc ctctttcact aatcctcctc agcacagacc 240
ctttacgggt gtcaggctgg gggacagtaa ggtctttccc ttcccacaag gccatatctc 300
aggetgtete agtgggggga aacettggae aataceeggg etttettggg e
<210> 349
<211> 207
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(207)
<223> n = A, T, C or G
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acagagtgag cgaaatgcag aagctggatg cacaggtcaa ggagctggtg ctgaagtcgg 180
cggtggaggc tgagcgcctg gtggctg
<210> 350
<211> 323
<212> DNA
<213> Homo sapiens
<400> 350
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tgggagccat tggctgtgaa gctgcagact tataagacag cagtggagac ggcagttctg 240
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<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(353)
<223> n = A, T, C or G
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ttgtccgttt ctgtggggtt aggtttatgt ttttaatcat ctgaggtcac gtctatttcc 180
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<210> 352
<211> 467
<212> DNA
<213> Homo sapiens
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aatttgagca gaacctgtct gagaaactct ctgaacaaga attacaattt cgtcgtctca 120
gtcaagagca agttgacaac tttactctgg atataaatac tgcctatgcc agactcagag 180
gaatcqaaca ggctgttcag agccatgcag ttgctgaaga ggaagccaga aaagcccacc 240
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ctactatccc gctgggtagt gcagttgagg ccatcaaagc caactgttct gataatgaat 360
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<210> 353
<211> 350
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<212> DNA
<213> Homo sapiens
<400> 353
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gaaatctgtc cccaccagga acagcccctg gaaaacggcc ccgtcctcta ccaccttgtg 120
gaaatgctgc acgggaactg cctcctggag gaccagcttt accttcccca gacatttgtc 180
ctgattgtgt agttttcctg gactgcattt caaattgact caggaactgt ttattgcatg 240
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ttgaagatgc ttcagatcca acaccaacaa gggcaaaccc ctttgactgg
<210> 354
<211> 351
<212> DNA
<213> Homo sapiens
<400> 354
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ttttaggttt tttgcttttc taatcaccaa ttcttatata caatgtatat tttagactcg 120
agcagatgat catcttcatc ttaagtcatt ccttttgact gagtatggca ggattagagg 180
gaatggcagt atagatcaat gtctttttct gtaaagtata ggaaaaacca gagaggaaaa 240
aaagagctga caattggaag gtagtagaaa attgacgata atttcttctt aacaaataat 300
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<211> 308
<212> DNA
<213> Homo sapiens
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ataaaaataa gaaattaagg gttaacatca atgtgccaat gaaaaccgaa cagaagcagg 180
aacaagaaac cacacaaa aacatcgagg aagaccgcaa actactgatt caqqcqqcca 240
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tcactcag
                                                                  308
<210> 356
<211> 207
<212> DNA
<213> Homo sapiens
<400> 356
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ggtactttga cgtggagagg aactcctgca ataacttcat ctatggaggc tgccggggca 180
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<210> 357
<211> 188
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
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<222> (1)...(188)
<223> n = A, T, C or G
<400> 357
togaccacgo cotogtagog catgngotho aggacgatgo toagagtgat gaacaccocg 60
gtgcggccca cgccagcact gcagtgcacc gtgataggcc catcctgtcc aaactgctcc 120
ttggtcttat gcacctgccc gatgaagtca atgaatccct cgcctgtctt gggcacgccc 180
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<211> 291
<212> DNA
<213> Homo sapiens
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aggcaggcgg tacgtgacag gggctgcatg caccggtggt cagagagaaa cagaacaggg 180
cagggaattt cacaatgttc ttctatacaa tggctggaat ctatgaataa catcagtttc 240
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<212> DNA
<213> Homo sapiens
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<223> n = A, T, C or G
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cccaaaaaaa ctcaaaaaang taatgaatga tacccaangn qccttttcta qaaaaaq 117
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<211> 394
<212> DNA
<213> Homo sapiens
<400> 360
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aagtttgccc cagctttccc gggcacacca ccttttgtcc caagtgtctq ccqqtcqacc 180
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ttqaaqagtg gcccttgag gccctggaaa gaccaatcac tggacttctt cccttgagag 300
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tcaagagaaa ctctgcaggg cactcccctg tttc
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<210> 361
<211> 394
<212> DNA
<213> Homo sapiens
<220>
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tqaqtctqtq qqataqctqc catqaaqtaa cctgaaqqaq qtqctqqctq qtaqqqttq 180
attacagggt tgggaacagc tcgtacactt gccattctct gcatatactg gttagtgagg 240
tgagcctggc gctcttcttt gcgctgagct aaagctacat acaatggctt tgtggacctc 300
qqccqcqacc acqctaaqcc gaattccaqc acactggcgg ccqttactag tgqatccqaq 360
ctcqgtacca agcttggcgt aatcatggtc atag
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<210> 362
<211> 268
<212> DNA
<213> Homo sapiens
<400> 362
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tgtttaagga tggtctcggt ggttaggccc actagaataa actgagtcca atacctctac 180
acagttatgt ttaactgggc tctctgacac cgggaggaag gtggcggggt ttaggtgttg 240
caaacttcaa tggttatgcg gggatgtt
<210> 363
<211> 323
<212> DNA
<213> Homo sapiens
<400> 363
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qtttqtaccc gttgatgata gaatggggta ctgatgcaac agttgggtag ccaatctgca 120
gacagacact ggcaacattg cggacaccct ccaggaagcg agaatgcaga gtttcctctg 180
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gcccaaagga gaagggggag atgttgagca tgttcagcag cgtggcttcg ctggctccca 300
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<210> 364
<211> 393
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(393)
<223> n = A, T, C or G
<400> 364
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cacccagggg cactggcatc gtctccgcac ctgtgcctaa gaagctgctc atgatggctg 180
gcatcgatga ctgctacacc tcagcccggg gctgcactgc caccctgggc aacttcgcca 240
aggecactt tgatgecatt tetaagacet acagetacet gaceceegae etetggaagg 300
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<211> 371
<212> DNA
<213> Homo sapiens
<400> 365
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cctgccttct gggagcactt gggacagagg aatccgctgc attcctgctg gtggacctcg 240
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<211> 393
<212> DNA
<213> Homo sapiens
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<210> 367
<211> 327
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(327)
<223> n = A, T, C or G
<400> 367
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gcagaacgat gcgggcattg tccacagtat ttgcgaagat ctgagccctc aggtcctcga 120
tgatcttgaa gtaatggctc cagtctctga cctggggtcc cttcttctcc aagtgctccc 180
ggattttgct ctccagcctc cggttctcgg tctccaggct cctcactctg tccaggtaag 240
aggecaggeg gtcgttcagg ctttgcatgg tctccttctc gttctggatg cctcccattc 300
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<210> 368
<211> 306
<212> DNA
<213> Homo sapiens
<220>
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<221> misc feature

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aacqqaqqca ctgtggccga gaagctggac tgggcccgcg agaggcttga gcaqcaqqta 180
cctgtgaacc aagtgtttgg gcaggatgag atgatcgacg tcatcggggt gaccaagggc 240
aaaggctaca aaggggtcac cagtcgttgg cacaccaaga agctgccccg caagacccac 300
cgagga
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<210> 369
<211> 394
<212> DNA
<213> Homo sapiens
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ccttqaaata cactgcqttg acgaggacca gtctqqtqaq cacaccatca ataaqatctq 180
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<211> 653
<212> DNA
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ctqqtqtcac agaqqctact attactgqcc tggaaccggg aaccgaatat acaatttatg 180
tcattqccct gaagaataat cagaagagcg agcccctgat tggaaggaaa aagacagacg 240
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ttccttccac agttcaaaag acceettteg teacecacee tgggtatgae actggaaatg 360
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<210> 371
<211> 268
<212> DNA
<213> Homo sapiens
<400> 371
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gctccacctg gactacatcg ggccttgcaa atacatcccc ccttgcctgg actctgagct 180
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<211> 392
<212> DNA
<213> Homo sapiens
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<210> 373
<211> 388
<212> DNA
<213> Homo sapiens
<220>
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<222> (1)...(388)
\langle 223 \rangle n = A, T, C or G
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aaccattggc ctgggccagc ttgcacgcct gaagagactc ggtcacggag ccaatctggt 180
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gccaagetee ccagteatee tggtcaaagg gatettegat agacaceaet gggtagteet 360
tgatgaagga cttgtacagg tcagccag
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<211> 393
<212> DNA
<213> Homo sapiens
<400> 374
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<211> 394
<212> DNA
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<220>
<221> misc_feature
<222> (1)...(394)
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<210> 376
<211> 392
<212> DNA
<213> Homo sapiens
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<222> (1)...(392)
<223> n = A, T, C or G
<400> 376
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<213> Homo sapiens
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<211> 223
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<213> Homo sapiens
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<210> 380
<211> 317
<212> DNA
<213> Homo sapiens
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<221> misc_feature
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<212> DNA
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<222> (1)...(392)
<223> n = A, T, C or G
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                                                                  2627
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<211> 310
<212> PRT
<213> Homo sapiens
<400> 392
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                                     10
Ser Thr Gln Ile Arg Trp Glu Pro Ser Pro Ala Met Ala Ser Leu Gly
             20
Gln Ile Leu Phe Trp Ser Ile Ile Ser Ile Ile Ile Ile Leu Ala Gly
```

Ala Ile Ala Leu Ile Ile Gly Phe Gly Ile Ser Gly Arg His Ser Ile

- 50 55 60

Thr Val Thr Thr Val Ala Ser Ala Gly Asn Ile Gly Glu Asp Gly Ile 65 70 75 80

Leu Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu Ser Asp Ile Val Ile 85 90 95

Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val His Glu Phe Lys Glu 100 105 110

Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met Phe Arg Gly Arg Thr 115 120 125

Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn Ala Ser Leu Arg Leu 130 135 140

Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr Lys Cys Tyr Ile Ile 145 150 155 160

Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu Tyr Lys Thr Gly Ala 165 170 175

Phe Ser Met Pro Glu Val Asn Val Asp Tyr Asn Ala Ser Ser Glu Thr 180 185 190

Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln Pro Thr Val Val Trp 195 200 205

Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser Glu Val Ser Asn Thr 210 215 220

Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met Lys Val Val Ser Val 225 230 235 240

Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser Cys Met Ile Glu Asn 245 250 255

Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val Thr Glu Ser Glu Ile 260 265 270

Lys Arg Arg Ser His Leu Gln Leu Leu Asn Ser Lys Ala Ser Leu Cys 275 280 285

Val Ser Ser Phe Phe Ala Ile Ser Trp Ala Leu Leu Pro Leu Ser Pro 290 295 300

Tyr Leu Met Leu Lys 305

<210> 393

<211> 283

<212> PRT

<213> Homo sapiens

<400>. 393 Met Ala Ser Leu Gly Gln Ile Leu Phe Trp Ser Ile Ile Ser Ile Ile Ile Ile Leu Ala Gly Ala Ile Ala Leu Ile Ile Gly Phe Gly Ile Ser 25 Gly Arg His Ser Ile Thr Val Thr Thr Val Ala Ser Ala Gly Asn Ile 40 Gly Glu Asp Gly Ile Leu Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu 55 Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn 105 Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr Lys Cys Tyr Ile Ile Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu 135 Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Val Asn Val Asp Tyr Asn 150 Ala Ser Ser Glu Thr Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln 170 Pro Thr Val Val Trp Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser 180 185 Glu Val Ser Asn Thr Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met Lys Val Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr..Tyr Ser 215 220 Cys Met Ile Glu Asn Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val 230 Thr Glu Ser Glu Ile Lys Arg Arg Ser His Leu Gln Leu Leu Asn Ser

250

Lys Ala Ser Leu Cys Val Ser Ser Phe Phe Ala Ile Ser Trp Ala Leu

280

BNSDOCID: <WO____0036107A2_I_>

275

Leu Pro Leu Ser Pro Tyr Leu Met Leu Lys

11729.1 contg

11729-45.21.21.cons1

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GAAGAAGATGCATTAA.A.A.T.A.TGGGTTA.TTTTCAACTTTTTATCTGAGGACA.AGTATCCAT
TAATTATTGTGTC.A.G.A.G.A.G.A.T.A.CCTGCTTAAGAAGCTT.A.CA.G.A.G.CTATGGAG
GAGGTTGGCAGC.A.G.A.C.A.T.T.G.A.C.A.TTATAAAATCAACTTTGATGACAGTAAAAATG
GCCTTTCTGCATGGGAACTTA.TTGAGCTTATTGGAAATGGACAGTTTAGCAAAGGCATGGA
CCGGCAGACTGTGTCTATGGCA.A.TTAATGAAGTCTTTAATGAACTTATATTAGATGTGTTA
AAGCAGGGTTA.CATGATGAA.A.A.A.GGGCCA.C.A.GACGGAAAAA.CTTGGACTGAAAGATGGTT
TGTACTAAAACCCAA.C.A.T.T.T.CTT.A.CTATGTGAGTGAGGATCTGAAGGATAAGAA.GG
AGACATTCTCTTGGATGAAAATTGCTGTGTAGAGTCCTTGCCTGACAAAGATGGAAA

11729-45.21.21.cons2

11731.1contig

11731.2contig

11734.1contig

11734.2contig

GCCAAGAAGCCCGAAAGGTGAAGCATCTGGATGGGGAAGAGGATGGCAGCAGTGATCA GAGTCAGGCTTCTGGAACCACAGGTGGCCGAAGGGTCTCAAAGGCCCTAATGGCCTCAAT GGCCCGCAGGGCTTCAAGGGTCCCATAGCCTTTTGGGCCCGCAGGGCATCAAGGACTCG GTTGGCTGCTTGGGCCCGGAGAGCCTTGCTCTCCCTGAGATCACCTAAAGCCCGTAGGGGC AAGGCTCGCCGTAGAGCTGCCAAGGTCATCCCAAGAGCCTGAAGCACCACCACCT CGGGATGTGGCCCTTTTGCAAGGGAGGGCAAATGATTTGGTGAAGTACCTTTTGGCTAAAG ACCAGACGAAGATTCCCATCAAGCGCTCGGACATGCTGAAGGACATCATCAAAGAATACA CTGATGTGTACCCCGGAAATCATTGAACGAGCAGGCTATTCCTTGGAGAAGGTATTTGGGAT

11736.1contg

11736.2contig

11739-182

11740.1.contig

11766.1.contig

11766.2.contig

II-3.2.contig

11-5-1&2

11777.1&2.cons

11779.2.contig

11781 & 37.cons

CTCTGTGGAAAACTGATGAGGAATGAATTTACCATTACCCATGTTCTCATCCCCAAGCAAA AGCAGGGCCTCATCACACTGGGCTGGATTCATACTCACCCCCACACAGACGGCGTTTCTCTC **CAGTGTCGACCTACACACTCACTGCTCTTACCAGATGATGTTGCCAGAGTCAGTAGCCATT** AGATTTCTTCCTGTCGCCAGAAAGGATTTCATCCACACAGCAAGGATCCACCTCTGTTCTG TAGCTGCAGCCACGTGACTGTTGTGGACAGAGCAGTGACCATCACAGACCTTCGATGAGC GTTTGAGTCCAACACCTTCCAAGAACAACAAAACCATATCAGTGTACTGTAGCCCCTTAAT TTAAGCTTTCTAGAAAGCTTTGGGAAGTTTTTGTAGATAGTAGAAAGGGGGGGCATCACXTGA GAAAGAGCTGATTTTGTATTTCAGGTTTGAAAAGAAATAACTGAACATATTTTTTAGGCAA GTCAGAAAGAGAACATGGTGACCCAAAAGCAACTGTAACTCAGAAATTAAGTTACTCAGA TGGATTCACCAATTGTTAACATTTTTTCTCTCTCAGCTATCCTTCTAATTTCTCTCTAATTTC AATTTGTTTATATTTACCTCTGGGCTCAATAAGGGCATCTGTGCAGAAATTTGGAAGCCAT TTAGAAAATCTTTTGGATTTTCCTGTGGTTTATGGCAATATGAATGGAGCTTATTACTGGG GTGAGGGACAGCTTACTCCATTTGACCAGATTGTTTGGCTAACACATCCCGAAGAATGATT TTGTCAGGAATTATTGTTA.TTAATAATAFTTCAGGATATTTTTCCTCTACAATAAAGTAA CAAT

11781-76-87-37

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11-8-182

1! 35.2.contig

11718-1&2 cons

13690.4

13693.1

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CCTCAGGTGATCCACCTGCCTCGGCCTCCCAAAGTGTTGGCTCCAGCCTGAGCTACCC
GTGCCTGGCCAGCCACTGGAGTTTAAAGGACAGTCATGTTGGCTCCAGCCTAAGGCGGCA
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13694.1

13694.2

92

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13695.1

13695.2

13697.1

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CATCCATATTCTGGGACTCAGGCGGGAACTTTCTGGAATATTGCCAGGGAGCATGGCAGA
GGGGCACAGTGCATCTCTGGGGGGAATGCACATTGGCTCAGCCTGGGTAATGAGTGATATAC
ATTACCTCTGTTCACAACTCATTGCCCAGCACCAGTCACAAGGCCCCACCAAATACCAGAG
CCCAAGAAATGTAGTCCTGTTGATATGGTTTTGCTGTGTCCCAACCCAAATCTCATCTTGA
ATTGTAAGCTCCCATAATTCCCATGTGTGTGGGAGGGACCTGGTG

FIG. 1H

E LA

13697.2

ATCATGAGGATGTTACCAAAGGGATGGTACTAAACCATTTGTATTCGTCTGTTTTCACACT
GCTTTGAAGATACTACCTGAGACTGGGTAATTTATAAACAAAAGAGATTTAATTGACTCAC
AGTTCTGCATGGCTGAAGAGGCCTCAGGAAACTTACAGTCATGGTGGAAGGCAAAGGAGG
AGCAAGGCATGTCTTACATGTCAGTAGGAGAGAGGCGAGAGCAGGAGAACCTGCCACTT
ATAAACCATTCAGATCTCATAACTCCCTATCATGAGAAAAACATGGAGGAAACCACCCTC
ATGATCCAATCACCTCCCGCCAGGTCCCTCCCTCGACACGTGGGGATTATAATTCAGGATT
AGAGGGACACAGAGACAAACCATATCATCATCATGAGAAATCCACCCTCATAGTCCAAT
CAGCTCCTACCAGGCCCCACCTCCAACACTGGGGATTGCAATTCAACATGAGATTTGGATG

13699.1&2

13703.3

13705.1

13707.4

13708.1&2

GGCGGGTAGGCATGGAACTGAGAAGAACGAAGAAGCTTTCAGACTACGTGGGGAAGAAT
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GCCTATTATTAGCAGTGAGGAGCAGAAGCAGCTGATGCTGTACTATCACAGAAGACAAGA
GGAGCTCAAGAGATTGGAAGAAAATGATGATGATGCCTATTTAAACTCACCATGGGCGGA
TAACACTGCTTTGAAAAGACATTTTCATGGAGTGAAAGACATAAAGTGGAGACCAAGATG
AAGTTCACCAGCTGATGACACCTTCCCAAAGAGATTAGCTCACCT

13709.1

TCTGAAGGTTAAATGTTTCATCTAAATACGGATAATGRTAAACACCTATAGCATAGAGTTG
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TTGTTGTTGATGATGATGATGATGATGATGATAATATTTTTCTATCCCCAGTGCACAACTGCTTG
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TGATGAAGCCCTACATTTTCTTCTAGAGGAGATGACATTTGAGCAAGATCTTAAAGAAAAT
CAGATGCCTTCACCTGGCCACTGCTTGGTGATCCCATGGCACTTTGTACATCTCTCCATTAG
CTCTCATCACCAGCCCATCATTATTGTATGTGTCTGCCTTCTTGAAGCTTGCAGCTGCCTAC
CATCMGGTAGAATAAAAATCATCCTTTCATAAAATAGTGACCCTCCTTTTTTATTTGCATTT

13712.1&2

13714.1&2

13716.1&2

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13722.3

CATGCGTTTCACCACTGTTGGCCAGGCTGGTCTCGAACTCCTGGCCTCAAGCAATCCACCC GCCTCAGCCTCAAAAGTGCTGGGATTACAGATGTGAGCCATGGCACATGCCAAAAGGC TATATTCCTGGCTCTGTTTCCGAGACTGCTTTTAATCCCAACTTCTCTACATTTAGATTA AAAAATATTTTATTCATGGTCAATCTGGAACATAATTACTGCATCTTAAGTTTCCACTGAT GTATATAGAAGGCTAAAGGCACAATTTTTATCAAATCTAGTAGAGTAACCAAACATAAAA TCATTAATTACTTTCAACTTAATAAAAAAATATTTGACATTCCTCAAAAGAGCTGTTTTCAATCCT GATAGGTTCTTTATTTTTCAAAATATATTTGCCATGGGATGCTAATTTGCAATAAAGAGCGCGC ATAATGAGAGAATACCCCCAAACTGGA

13722.4

13-148-13698-13748

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CCAFAGAGAACGTCAAAGCAAAGATCCARGACAAGGAAGGCRTYCCTCCTGACCAGCAGA
GGTTGATCTTTGCCGGAAAGCAGCTGGAAGATGGDCGCACCCTGTCTGACTACAACATCC
AGAAAGAGTCYACCCTGCACCTGGTGCTCCCGTCTCAGAGGTGGGATGCARATCTTCGTGA
AGACCCTGACTGGTAAGACCATCACCCTCGAGGTGGAGCCCAGTGACACCATCGAGAATG
TCAAGGCAAAGATCCAAGATAAGGAAGGCATCCCTCCTGATCAGCAGAGGTTGATCTTTG
CTGGGAAACAGCTGGAAGATGGACGCACCCTGTCTGACTACAACATCCAGAAAGAGTCCA
CTCTGCACTTGGTCCTGCGCTTCGAGGGGGGGGTGTCTAAGTTTCCCCTTTTTAAGGTTTCMAC
AAATTTCATTGCACTTTCCTTTCAATAAAGTTGTTGCATTCCC

13732.1

13732.2

....

13735.1

13735.2

13736.1

AGAATCCATTTATTGGGTTTTAAACTAGTTACACACACTGAAATCAGTTTGGCACTACTTTA
TACAGGGATTACGCCTGTGTATGCCGACACTTAAATACTGTACCAGGACCACTGCTGTGCT
TAGGTCTGTATTCAGTCATTCAGCATGTAGATACTAAAAATATACTGTAGTGTTCCTTTAA
GGAAGACTGTACAGGGTGTGTTGCAAGATGACATTCACCAATTTGTGAATTATTTCAACCC
AGAAGATACCTTTCACTCTATAAAACTTGTCATAGGCAAACATGTGGGTGTTAGCATTGAGAG
ATGCACACAAAAATGTTACATAAAAGTTCAGACATTCTAATGATAAGTGAACTGAAAAAA
AAAAAAACCCCACATCTCAATTTTTGTAACAAGATAAAGAAAATAATTTAAAAAACACAAA
AAATGGCATTCAGTGGGTACAAAGCC

13737.132

FIG. 1N

TTTGACTITAGTAGGGGTCTGAACTATTTATTTTACTTTGCCMGTAATATTTARACCYTATA
TATCTTTCATTATGCCATCTTATCTTCTAATGBCAAGGGAACAGWTGCTAAMCTGGCTTCT
GCATTWATCACAITAAAAATGGCTTTCTTGGAAAATCTTCTTGATATGAATAAAGGATCTT
TTAVAGCCATCATTTAAAGCMGGNTTCTCTCCAACACGAGTCTGCTSASGGGGGGKGAGCT
GTGAACTCTGGCTGAAGGCTTTCCCATACACACTGCAATGACMTGGTTTCTGACCAGBGTG
AGTTA

13738.2

13730.1&2

13741.1

· -

14351.1

14351.2

ACCTTAAAGACATAGGAGAATTTATACTGGGAGAGAAAGCTTACAAATGTAAGGTTTCTG ACAAGACTTGGGAGTGATTCACACCTGGAACAACATACTGGACTTCACACTGGABAGAAA CCTTACAAGTGTAATGAGTGTGGCAAAGCCTTTGGCAAGCAGTCAACACTTATTCACCATC AGGCAATTCA

14354.2

AGTCAGGATCATGATGGCTCAGTTTCCCACAGCGATGAATGGAGGGCCAAATATGTGGGC
TATTACATCTGAAGAACGTACTAAGCATGATAAACAGTTTGATAACCTCAAACCTTCAGGA
GGTTACATAACAGGTGATCAAGCCGGTACTTTTTCCTACAGGTCAGGTCTGCCGGCCCCGG
TTTTAGCTGAAATATGGGCCTTATCAGATCTGAACAAGGATGGGAAGATGGACCAGCAAG
AGTTCTCTATAGCTATGAAACTCATCAAGTTAAAGTTGCAGGGCCAACAGCTGCCTGTAGT
CCTCCCTCCTATCATGAAACAACCCCCTATGTTCTCCCACTAATCTCTGCTCGTTTTGGGA
TGGGAAGCATGCCCAATCTGTCCATCATCAGCCATTGCCTCCACTTATAGCAAC
ACCCTTGTCTTCTGCTACTTCAGGGGACCAGTATTCCTCCCCTAATGATGCCTCCT

14354.1

16431.1.2

16432-1

16432-2

171843

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TTAACTGAAATAGCGTCCATCCAAAAGTGGGTTTAAGGTAAAACTAAGTCACGATATTGGC
GGGGATCCTGCAGTTTGGACTGCTTGCCGGGTTTGTCCAGGGTTCCGGGTCTGTTCTTGGC
ACTCATGGGGACAGGCATCCTGCTCGTCTGTGGGGGCCCCGCTGGAGCCCTTACGTGAAGCT
GAAGGTATCGACCSTAGGGGGCTCTAGGGCAGTGGGGACCCTTCATCCGGAACTAACAAGGG
TCGGGGAGAGGCCTCTTGGGGCTATGTGGG

FIG. 1Q

CAAGCGTTCCTTTATGGATGTAAATTCAAACAGTCATGCTGAGCCATCCCGGGCTGACAGT CACGTTWAAGACACTAGGTCGGGCGCCACAGTGCCACCCAAGGAGAAGAAGAATTTGGA ATTTTTCCATGAAGATGTACGGAAATCTGATGTTGAATATGAAAATGGCCCCCAAATGGAA TTCCAAAAAGGTTACCACAGGGGCTGTAAGACCTAGTGACCCTCCTAAGTGGGAAAGAGGA ATGGAGAATATCTGATGCATCAAGACATCAGAATATAAAACTGAGATCATAATG AAGGAAAATTCCATATCCAATATGAGAAAATTCCCAATATCCAAGA

17185.1

TAGGAATAACAAATGTTTATTCAGAAATGGATAAGTAATACATAATCACCCTTCATCTCTT
AATGCCCCTTCCTCTCTCTGCACAGGAGACACAGATGGGTAACATAGAGGCATGGGAA
GTGGAGGAGACACAGGACTAGCCCACCACCTTCTCTCTCCCGGTCTCCCAAGATGACTGCT
TATAGAGTGGAGGAGGCAAACAGGTCCCCTCAATGTACCAGATGGTCACCTATAGCACCA
GCTCCAGATGGCCACGTGGTTGCAGCTGGACTCAATGAAACTCTGTGACAACCAGAAGAT
ACCTGCTTTGGGATGAGAGGGAGGATAAAGCCATGCAGGGAGGATATTTACCATCCCTAC
CCTAAGCACAGTGCAAGCAGTGAGCCCCCGGCTCCCAGTACCTGAAAAAACCAAGGCCTAC

17183.2

1-190.1

17191.2&89.2

TGGCCTGGGCAGGATTGGGAGAGAGAGGTAGCTACCCGGATGCAGTCCTTTGGGATGAAGAC
TATAGGGTATGACCCCATCATTTCCCCAGAGGTCTCGGCCTCCTTTGGTGTTGAGCAGCTG
CCCCTGGAGGAGATCTGGCCTCTCTGTGATTTCATCACTGTGCACACTCCTCTCCTGCCCTC
CACGACAGGCTTGCTGAATGACAACACCTTTGCCCAGTGCAAGAAGGGGGTGCGTGTGGT
GAACTGTGCCCGTGGAGGGATCGTGGACGAAGGCGCCCTGCTCCGGGCCCTGCAGTCTGG
CCAGTGTGCCGGGGCTGCACTGGACGTGTTTACGGAAGAGCCGCCACGGGACCGGGCCTT
GGTGGACCATGAGAATGTCATCAGCTGTCCCCACCTGGGTGCCAGCACCAAGGAGGCTCA
GAGCCGCTGTGGGGAGGAAATTGCTGTTCAGTTCGTGGACATGGTGAAGGGGAAATCTCT

FIG. 1S

AGCCAGATGGCTGAGAGCTGCAAGAAGAAGTCAGGATCATGATGGCTCAGTTTCCCACAG CGATGAATGGAGGGCCAAATATGTGGGCTATTACATCTGAAGAACGTACTAAGCATGATA AACAGTTTGATAACCTCAAACCTTCAGGAGGTTACATAACAGGTGATCAAGCCCGTACTTT TTTCCTACAGTCAGGTCTGCCGGCCCCGGTTTTAGCTGAAATATGGGCCTTATCAGATCTG **AACAAGGATGGGAAGATGGACCAGCAAGAGTTCTCTATAGCTATGAAACTCATCAAGTTA** AAGTTGCAGGGCCAACAGCTGCCTGTAGTCCTCCCTATCATGAAACAACCCCCTATGT TCTCTCCACTAATCTCTGCTCGTTTTGGGATGGGAAGCATGCCCAATCTGTCCATTCATCAG CCATTGCCTCCAGTTGCACCTATAGCAACACCCTTGTCTTCTGCTACTTCAGGGACCAGTAT TCCTCCCCTAATGATGCCTGCTCCCCTAGTGCCTTCTGTTAGTACATCCTCATTACCAAATG GAACTGCCAGTCTCATTCAGCCTTTATCCATTCCTTATTCTTCTTCAACATTGCCTCATGCA TCATCTTACAGCCTGATGATGGGAGGATTTGGTGGTGCTAGTATCCAGAAGGCCCAGTCTC TGATTGATTTAGGATCTAGTAGCTCAACTTCCTCAACTGCTTCCCTCTCAGGGAACTCACCT AAGACAGGGACCTCAGAGTGGGCAGTTCCTCAGCCTTCAAGATTAAAGTATCGGCAAAAA TTTAATAGTCTAGACAAAGGCATGAGCGGATACCTCTCAGGTTTTCAAGCTAGAAATGCCC TTCTTCAGTCAAATCTCTCTCAAACTCAGCTAGCTACTATTTGGACTCTGGCTGACATCGAT GGTGACGGACAGTTGAAAGCTGAAGAATTTATTCTGGCGATGCACCTCACTGACATGGCC AAAGCTGGACAGCCACTACCACTGACGTTGCCTCCGAGCTTGTCCCTCCATCTTTCAGAG GGGGAAAGCAAGTTGATTCTGTTAATGGAACTCTGCCTTCATATCAGAAAACACAAGAAG AAGAGCCTCAGAAGAAACTGCCAGTTACTTTTGAGGACAAACGGAAAGCCAACTATGAAC GAGGAAACATGGAGCTGGAGAAGCGACGCCAAGTGTTGATGGAGCAGCAGCAGAGGGAG GCTGAACGCAAAGCCCAGAAAGAGAAGAAGAGTGGGAGGGGAAACAGAGAGAACTGC AACAGGAGCTTGAGAGACAACGCCGTTTAGAATGGGAAAGACTCCGTCGGCAGGAGCTGC CTCCACCTGGAACTGGAAGCAGTGAATGGAAAACATCAGCAGATCTCAGGCAGACTACAA GATGTCCAAATCAGAAAGCAAAACACAAAAAGACTGAGCTAGAAGTTTTGGATAAACAGTGT GACCTGGAAATTATGGAAATCAAACAACTTCAACAAGAGCTTAAGGAATATCAAAATAAG CTTATCTATCTGGTCCCTGAGAAGCAGCTATTAAACGAAAGAATTAAAAACATGCAGCTCA GTAACACACCTGATTCAGGGATCAGTTTACTTCATAAAAAGTCATCAGAAAAGGAAGAAT TATGCCAAAGACTTAAAGAACAA TTAGATGCTCTTGAAAAAGAAACTGCATCTAAGCTCT CAGAAATGGATTCATTTAACAAFCAGCTGAAGGAACTCAGAGAAAGCTATAATACACAGC AGTTAGCCCTTGAACAACTTCATAAAATCAAACGTGACAAATTGAAGGAAATCGAAAGAA AAAGATTAGAGCAAAAAAAAAAA

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FIG. 2B

ATATCTAGAAGTCTGGAGTGAGCAAACAAGAGCAAGAAACAAAAAGAAGCCAAAAGCAG AAGGCTCCAATATGAACAAGATAAATCTATCTTCAAAGACATATTAGAAGTTGGGAAAAT AATTCATGTGAACTAGACAAGTGTGTTAAGAGTGATAAGTAAAATGCACGTGGAGACAAG TGCATCCCCAGATCTCAGGGACCTCCCCCTGCCTGTCACCTGGGGAGTGAGAGGACAGGAT AGTGCATGTTCTTTGTCTCTGAATTTTTAGTTATATGTGCTGTAATGTTGCTCTGAGGAAGC CCCTGGAAAGTCTATCCCAACATATCCACATCTTATATTCCACAAATTAAGCTGTAGTATG ATGGGTCAAATGATTCACTTTTTATGATGCTTCCAAAGGTGCCTTGGCTTCTCTTCCCAACT GACAAATGCCAAAGTTGAGAAAAATGATCATAATTTTAGCATAAACAGAGCAGTCGGCGA CAGATGATGTTCATCCGTGAATGGTCCAGGGAAGGACCTTTCACCTTGACTATATGGCATT ATGTCATCACAAGCTCTGAGGCTTCTCCTTTCCATCCTGCGTGGACAGCTAAGACCTCAGT TTTCAATAGCATCTAGAGCAGTGGGACTCAGCTGGGGTGATTTCGCCCCCCATCTCCGGGG GAATGTCTGAAGACAATTTTGTTACCTCAATGAGGGAGTGGAGGAGGATACAGTGCTACT ACCAACTAGTGGATAAAGGCCAGGGATGCTGCTCAACCTCCTACCATGTACAGGACGTCTC CCCATTACAACTACCCAATCCGAAGTGTCAACTGTGTCAGGACTAAGAAACCCTGGTTTTG ATTGGCAAATAAGCATTCTGTCTCTTTGGCTGCTGCCTCAGCACAGAGAGCCAGAACTCTA TCGGGCACCAGGATAACATCTCTCAGTGAACAGAGTTGACAAGGCCTATGGGAAATGCCT CCAAGTTCTGTAAGAGAAATGCCTGAGTTCTAGCTCAGGTTTTCTTACTCTGAATTTAGATC CACACAGACTTTTGAAAGCAAGGACAATGACTGCTTGAATTGAGGCCTTGAGGAATGAAG CTTTGAAGGAAAAGAATACTTTGTTTCCAGCCCCCTTCCCACACTCTTCATGTGTTAACCAC TGCCTTCCTGGACCTTGGAGCCACGGTGACTGTATTACATGTTGTTATAGAAAACTGATTTT AGAGTTCTGATCGTTCAAGAGAATGATTAAATATACATTTCCTA

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AGCGTGGTCGCGGCCGAGGTGTCCTTCAGGGTCTGCTTATGCCCTTGTTCAAGAACACCAG TGTCAGCTCTCTGTACTCTGGTTGCAGACTGACCTTGCTCAGGCCTGAGAAGGATGGGGCA GCCACCAGAGTGGATGCTGTCTGCACCCATCGTCCTGACCCCAAAAGCCCTGGACTGGACA GAGAGCGGCTGTACTGGAAGCTGAGCCAGCGCATCACTGAGCTGGGCCCCT ACACCCTGGACAGGGACAGTCTCTATGTCAATGGTTTCACCCATCGGAGCTCTGTACCCAC CACCAGCACCGGGGTGGTCAGCGAGGAGCCATTCAACCTGCCCGGGCCGCTCGA

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BAGCGTGGTCGCGGGCCGAGGTCCAGTCGCAGCATGCTCTTTCTCCTGCCCACTGGCACAGTG
AGGAAGATCTCTGCTGTCAGTGAGAAGGCTGTCATCCACTGAGATGGCAGTCAAAAGTGC
ATTTAATACACCTAACGTATCGAACATCATAGCTTGGCCCAGGTTATCTCATATGTGCTCA
GAACACTTACAATAGCCTGCAGACCTGCCCGGGCGGCCGCTCGA

TGTGGTGTTGAACTTCCTGGAGNCAGGGTGACCCATGTCCTCCCCATACTGCAGGTTGGTG
ATGGTGAAGTTGAGGTGAATGGTACCAGGAGAGGGCCAGCAGCCATAATTGTSGRGCKG
SMGMSSGAGGMWGGWGTYYCWGAGGTTCYRARRTCCACTGTGGAGGTCCCAGGAGTGCT
GGTGGTGGGGACAGAGSTCYGATGGGTGAAACCATTGACATAGAGACTGTTCCTGTCCAG
GGTGTAGGGGCCCAGCTCTTYRATGYCATTGGYCAGTTKGCTYAGCTCCCAGTACAGCCRC
TCTCKGYYGMGWCCAGSGCTTTTGGGGTCAAGATGATGCAGTGCAGCATCCACTCCA
GTGGCTGCTCCATCCTTCTCGGACCTGAGAGAGGGTCAGTCTGCAGCCAGAGTACAGAGGG
CCAACACTGGTGTTCTTTGAATA

TCGAGCGGCCGCCGGGCAGGTCAGGAAGCACATTGGTCTTAGAGCCACTGCCTCCTGGA TTCCACCTGTGCTGCGGACATCTCCAGGGAGTGCAGAAGGGAAGCAGGTCAAACTGCTCA GATCAGTCAGACTGGCTGTTCTCAGTTCTCACCTGAGCAAGGTCAGTCTGCAGCCAGAGTA CAGAGGGCCAACACTGGTGTTCTTGAACAAGGGCTTGAGCAGACCCTTGCAGAACCCTCTTC CGTGGTGTTTGAACTTCCTGGAAACCAGGGTGTTGCATGTTTTTCCTCATAATGCAAGGTTG

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11721-2

117241

TITGTTCCTTACATTTTCTAAAGAGTTACTTAAATCAGTCAACTGGTCTTTGAGACTCTTA
AGTTCTGATTCCAACTTAGCTAATTCATTCATTCTGAGACACTGTGGTATAGGTGGCGTGTCTCTTC
TAGCTGGGACAAAAGTTCTTTGTTTTCCCCCCTGTAGAGTATCACAGACCTTCTGCTGAAGC
TGGACCTCTGTCTGGGCCTTGGACTCCCAAATCTGCTTGTCATGTTCAAGCCTGGAAATGTT
AATCTTAATTCTTCCATATGGATGGACATCTGTCTAAGTTGATCCTTTAGAACACTGCAAT
TATCTTCTTTGAGTCTAATTTCTTCTTCCCTGCAGGTAAACTTCCTCTCCC
ATTCTTAGCTTCATCTATCACCCTGTCACGATCATCCTGGAGGGAAGACATGCTCTTAGTA
ATTCTTAGCTTCATCTATCACCCTGTCACGATCATCCTGGAGGGAAGACATGCTCTTAGTA
CTTTCTTGTTCAAAGTAACCTGAATCTCTCCCAAGTTTTCCTGAAGTTGCTGAACTTCCTTGT
GCAAAGCATCCAG

117242

FIG. 15.4

11725-32-1.2

11726-1&2

11727-1&2

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11728.1.40.19.19

11728.2.40.19.19

CCCGTGGGTGCCATCCACGGAGTTGTTACCTGATCTTTGGAAGCAGGATCGCCCGTCTGCACTGCAGTGGGAAGCCCGTGGGAGCAGTGATGGCATCCCCGCATGCCACGGCCTCTGGGAAGGGGCAGCAGCAGCAGTGATGGCATGCCACGGCCTCTGGGAAGGGGCAGCAACTGGAAGTCCCTGAGACCGTAAAGATGCAGGAGTGGCCGCAGAGCAGTGGGCATCAACCTGGCAGGGAGCACCCAGATGCCTCCAGTGTTGTGGGCCATTTGTCCAGAAGTGGACCATCTGGGCACCGGGTTCCAGGCAGCAGCAGCAACCAAGGGAAACTGACCATCTGGGCACCGCGTTCCAGCCACCAGCCTGCTGTTAAGGCCACCCAGCTCACCAGGGTCCACATGGTCCAATGGTCCCAATGGTCCAATGGTCCAATGGCCACCTGCTGTGAGCCACCTGCTGTGAGCCACCTGCTGTGAGCCACCTGCTGCTGCCCAATGCCCAACGCCACCTGCTGCCCAATGCCCAACGCCACCTGCTCCCCAAGGACAACTATGCCCAAGGCACCTGCTCCCCAAGGAAACTATGCCCAAGGCACCTGCTCCCCAAGGAAACTA

11730-1

11730-2

FIG. 15C

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11732.1contig

11732.2contig

11735-1-2

AGATCAACCTCTGCTGGTCAGGAGGAATGCCTTCCTTGTCTTGGATCTTTGCTTTGACGTTC
TCGATAGTRWCA2CTKXRYTSRAMSKMAAGKGYRATGRWMTTKSYWGWRASYXTMWWM
RSGRARAYTT12G1CAYCCCMCCTCW1AG2CGSAGKACCARGTGCA4A9GTGGACTCTTTCTG
GATGTTGTAGTCAGACAGGGTGCGTCCATCTTCCAGCTGTTTCCCAGCAAAGATCAACCTC
TGCTGATCAGGAGGGATGCCTTCCTTATCTTGGATCTTTGCCTTGACATTCTCGATGGTGTC
ACTGGGCTCCACCTCGAGGGTGATGGTCTTACCAGTCAGGGTCTTCACGAAGATYTGCATC
CCACCTCTGAGACGGAGCACCAGGTGCAGGGTRGACTCTTTCTGGATGTTGTAGTCAGACA
GGGTGCGYCCATCTTCCAGCTGCTTTCCS1GCAAAGATCAACCTCTGCTGGTCAGGAGGRAT
GCCTTCCTTGTCYTGGATCTTTGCYTTGACRTTCTCRATGGTGTCACTCGGCTCCACTTCGA
GAGTGATGGTCTTACCAGTCAGGGTCTTCCACGAAGATCTCCCACCTCTAA

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FIG. 15D

11765.2&64.2.contig

CGCCTCCACCATGTCCATCAGGGTGACCCAGAAGTCCTACAAGGTGTCCACCTCTGGCCCC CGGGCCTTCAGCAGCCGCTCCTACACGAGTGGGCCCGGTTCCCGCATCAGCTCCTCGAGCT TCTCCCGAGTGGGCAGCAGCAACTTTCGCGGTGGCCTGGGCGGCGGCTATGGTGGGGCCA GCGGCATGGGAGGCATCACCGCAGTTACGGTCAACCAGAGCCTGCTGAGCCCCCTTGTCCT GGAGGTGGACCCCAACATCCAGGCCGTGCGCACCCAGGAGAAGGAGCAGATCAAGACCCT CAACAACAAGTTTGCCTCCTTCATAGACAAGGTACGGTTCCTGGAGCAGCAGAACAAGAT GCTGGAGACCAAGTGGAGCCTCCTGCAGCAGCAGAAGACGGCTCGAAGCAACATGGACA ACATGTTCGAGAGCTACATCAACARCCTTAGGCGGCAGCTGGAGACTCTGGGCCAGGAGA AGCTGAAGCTGGAGCGGAGCTTGGC.4ACATGCAGGGGCTGGTGGAGGACTTCAAGAAC **AAGTATGAGGATGAGATCAATAAGCGTACAGAGATGGAGAACGAATTTGTCCTCATCAAG** AAGGATGTGGATGAAGCTTACATGAACAAGGTAGAGCTGGAGTCTCGCCTGGAAGGGCTG ACCGACGAGATCAACTTCCTCAGGCAGCTGTATGAAGAGGAGATCCGGGAGCTGCAGTCC CAGATCTCGGACACATCTGTGGTGCTGTCCATGGACAACAGCCGCTCCCTGGACATGGACA GCATCATTGCTGAGGTCAAGGCACAGTACGAGGATATTGCCAACCGCAGCCGGGCTGAGG CTGAGAGCATGTACCAGGTCAAGTATGAGGĀGCTGCAGAGCCTGGCTGGGAAGCACGGGG ATGACCTGCGGCGCACAAAGACTGAGATCTCTGAGATGAACCCGGAACATCAGCCCGGCT XCAGGCTGAGATTGAGGGCCTCAAAGGCCAGAXGGCTTXCCTGGAXGXCCGCCAT

11767.2.contig

11768-132

GGGAATGCAACACTITATTGAAAGGAAAGTGCAATGAAATTTGTTGAAACCTTAAAAGG
GGAAACTTAGACACCCCCCTCRAgCGMAGKACCARGTGCARAgGTGGACTCTTTCTGGAT
GTTGTAGTCAGACAGGGTRCGWCCATCTTCCAGCTGTTTYCCRGCAAAGATCAACCTCTGC
TGATCAGGAGGRATGCCTTCCTTATCTTGGATCTTTGCCTTGACATTCTCGATGGTGTCACT
GGGCTCCACCTCGAGGGTGATGGTCTTACCAGTCAGGGTCTTCACGAAGATYTGCATCCCA
CCTCTGAGACGGAGCACCAGGTGCAGGGTRGACTCTTTCTGGATGTTGTAGTCAGACAGG
CTTCCTTGTCYTGGATCTTTCCS&GCAAAGATCAACCTCTGCTGGTCAGGAGGRATGC
CTTCCTTGTCYTGGATCTTTGCYTTGACRTTCTCAATGGTGTCACTCGGCTCCACTTCGAGA
GTGATGGTCTTACCAGTCAGGGTCTTCACGAAGATCTGCATCCCACCTCTAAGACGGAGCA
CCAGGTGCAGGGTGGACTCTTTCTGGATGTTAGTCAGACAGGGTGCGTCCATCTTCCA
GCTGTTTTCCCAGCAAAGATCAACCT

11768-1&2-11735-1&2

AGGTTGATCTTTGCTGGGAAACAGCTGGAAGATGGACGCACCCTGTCTGACTACAAcCATC
CAGAAAGAGTCCACCCTGCACCTGGTGCTCCGTCTTAGAGGTGGATGCAGATCTTCGTGA
AGACCCTGACTGGTAAGACCATCACTCTCGAAGTGGAGCCGAGTGACACCATTGAGAAYG
TCAARGCAAAGATCCARGACAAGGAAGGCATYCCTCCTGACCAGCAGAGGTTGATCTTTG
CISGGAAAgCAGCTGGAAGATGGRCGCACCCTGTCTGACTACAACATCCAGAAAGAGTCYA
CCCTGCACCTGGTGCTCCGTCTCAGAGGTTGGATGCARATCTTCGTGAAGACCCTGACTGG
TAAGACCATCACCCTCGAGGTGGAGCCCCAGTGACACCATCGAGAATGTCAAGGCAAAGAT
CCAAGATAAGGAAGGCATCCCTCCTGATCAGCAGAGGTTGATCTTTGCTGGGAAACAGCT
GGAAGATGACGCACCCTGTCTGACTACAACATCCAGAAAGAGTCCACCTYTGCACYTGGT
MCTBCGICTY3GAGGKGGGRTGc22aTCTWMGTKWagaCaCiCaCTKKYAAGRYYaTCAMCMWi
gAKKTCgAKYSCASTKWCaCTWTCRAKAAMGTYRWWGCAWagaTCCMAGACAAGGAAGGAC
ATTCCTCCTGACCAGGAGAGTTGATCT

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1 i 69.2.contig

11-70.1.contig

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FIG. 15F

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11778.1.contig

11778-2&30-2

FIG. 15G

11782.1.contig

ATCTACGTCATCAATCAGGCTGGAGACACCATGTTCAATCGAGCTAAGCTGCTCAATATTG
GCTTTCAAGAGGCCTTGAAGGACTATGATTACAACTGCTTTGTGTTCAGTGATGTGGACCT
CATTCCGATGGACGACCGTAATGCCTACAGGTGTTTTTCGCAGCCACGGCACATTTCTGTT
GCAATGGACAAGTTCGGGTTTAGCCTGCCATATGTTCAGTATTTTTGGAGGTTGTGTCTCTC
CAGTAAACAACAGTTTCTTGCCATCAATGGATTCCCTAATAATTATTGGGGTTGGGGAGGA
GAAGATGACGACATTTTTAACAGATTAGTTCATAAAGGCATGTCTATATCACGTCCAAATG
CTGTAGTAGGGAGGTGTCGAATGATCCGGCATTCAAGAGACAAGAAAAATGAGCCCAATC
CTCAGAGGTTTGACCGGATCGCACATACAAAGGAAACGATGCGCTTCGATGGTTTGAACT
CACTTACCTACAAGGTGTTGGATGTCAGAGATACCCGTTATATACCCAAATCAC

11782.2.contig

11783-1 & 2

11786.1.contig

11786.2.contig

13691.1&2

13692.132

TCCGAATTCCAAGCGAATTATGGACAAACGATTCCTTTTAGAGGATTACTTTTTCAATTTC
GGTTTTAGTAATCTAGGCTTTGCCTGTAAAGAATACAACGATGGATTTTAAATACTGTTTG
TGGAATGTGTTTAAAGGATTGATTCTAGAACCTTTGTATATTTGATAGTATTTCTAACTTTC
ATTTCTTTACTGTTTGCAGTTAATGTTCATGTTCATGCTATGCAATCGTTTATATGCACGTTTC
TTTAATTTTTTTAGATTTTCCTGGATGTATAGTTTAAACAACAAAAAGTCTATTTAAAACTG
TAGCAGTAGTTTACAGTTCTAGCAAAGAGGAAAGTTGTGGGGGTTAAACTTTGTATTTTCTT
TCTTATAGAGGCTTCTAAAAAGGTATTTTATATATGTTCTTTTTAACAAATATTGTGTACAAC
CTTTAAAACATCAATGTTTGGATCAAAACAAGACCCAGCTTATTTTCTGC

13693.2

TGTGGTGGCGCGGGCTGAGGTGGAGGCCCAGGACTCTGACCCTGCCTTCAGCAA
GGCCCCCGGCAGCGCCGCCACTACGAACTGCCGTGGGTTGAAAAATATAGGCCAGTAAA
GCTGAATGAAATTGTCGGGAATGAAGACACCGTGAGCAGGCTAGAGGTCTTTGCAAGGGA
AGGAAATGTGCCCAACATCATCATTGCGGGCCCTCCAGGAACCGGCAAGACCACAAGCAT
TCTGTGCTTGGCCCGGGCCCTGCTGGGCCCAGCACTCAAAGATGCCATGTTGGAACTCAAT
GCTTCAAATGACAGGGGCATTGACGTTGTGAGGAATAAAATTAAAATGTTTGCTCAACAA
AAAGTCACTCTTCCCAAAGGCCGACATAAGATCATCATCTTGGATGAAGCAGCATG
ACCGACGGAGCCCAGCAAGCCTTGAGGAGAACCATGGAAATCTACTCTAAAACCACTCGT
TCGCCCTTGCTTGTAATGCTTCGGATAAGATCATCTGGAGCC

13696.1-13744.1

13700.1

CAAGGGATATATGTTGAGGGTACRGRGTGACACTGAACAGATCACAAAGCACGAGAAACA
TTAGTTCTCCCCCCCAGCGTCTCCTTCGTCTCCCTGGTTTTCCGATGTCCACAGAGTGA
GATTGTCCCTAAGTAACTGCATGATCAGAGTGCTGKCTTTATAAGACTCTTCATTCAGCGT
ATCCAATTCAGCAATTGCTTCATCAAATGCCGTTTTTGCCAGGCTACAGGCCTTTTCAGGA
GAGTTTAGAATCTCATAGTAAAAGACTGAGAAATTTAGTGCCAGACCAAGACGAATTGGG
TGTGTAGGCTGCATTNCTTTCTTACTAATTTCAAATGCTTCCTGGTAAGCCTGCTGGGAGTT
CGACACAAGTGGTTTGTTTGTTGCTCCAGATGCCACTTCAGAAAGATACCTAAAATAATCT
CCTTTCATTTTCAAAGTAGAACAC

13700.2

13701.1

13702.2

AGCTGGCGCTAGGGCTCGGTTGTGAAATACAGCGTRGTCAGCCCTTGCGCTCAGTGTAGAA
ACCCACGCCTGTAAGGTCGGTCTTCGTCCATCTGCTTTTTTCTGAAATACACTAAGAGCAG
CCACAAAACTGTAACCTCAAGGAAACCATAAGCTTGGAGTGCCTTAATTTTTAACCAGTT
TCCAATAAAACGGTTTACTACCT

13704.2-13740.2

GGAGATGAAGATGAGGAAGCTGAGTCAGCTACGGGCARGCGGGCAGCTGAAGATGATGA GGATGACGATGTCGATACCAAGAAGCAGAAGACCGACGAGGATGACTAGACAGCAAAAA AGGAAAAGTTAAA

13706.1

GATGAAAATTAAATACTTAAATTAATCAAAAGGCACTACGATACCACCTAAAACCTACTG CCTCAGTGGCAGTAKGCTAAKGAACATCAAGCTACAGSACATYATCTAATATGAATGTTA GCAATTACATAKCARGAAGCATGTTTGCTTTCCAGAAGACTATGGNACAATGGTCATTWG GGCCCAAGAGGATATTTGGCCNGGAAAGGATCAAGATNAANGTAAAG

.13706.2

13707_3

13710.2

AGGTTGGAGAAGGTCATGCAGGTGCAGATTGTCCAGGSKCAGCCACAGGGTCAAGCCCAA
CAGGCCCAGAGTGGCACTGGACAGACCATGCAGGTGATGCAGCCAGATCATCACTAACACA
GGAGAGATCCAGCAGATCCCGGTGCAGCTGAATGCCGGCCAGCTGCAGTATATCCGCTTA
GCCCAGCCTGTATCAGGCACTCAAGTTGTGCAGGACAGATCCAGACACTTGCCACCAAT
GCTCAACAGATTACACAGACAGAGGTCCAGCAAGGACAGCAGCAGTTCAAGCCAGTTCAC
AAGATGGACAGCAGCTCTACCAGATCCAGCAAGTCACCATGCCTGCGGGCCANGACCTCG
CCAGCCCATGTTCATCCAGTCAAGCCAACCAGCCCTTCNACGGGCAGGCCCCCAGGTGAC
CGGCGACTGAAGGGCCTGAGCTGGCAAGGCCAACACAATTTTTGCCATAC
AGCCCCCAAGGCAATGGGCAACCAGCCTTTCCCCAGAGGAC

13710-1

TGAGATTTATTGCATTTCATGCAGCTTGAAGTCCATGCAAAGGRGACTAGCACAGTTTTTA
ATGCATTTAAAAAATAAAAGGGAGGTGGGCAGCAAACACACAAAGTCCTAGTTTCCTGGG
TCCCTGGGAGAAAAGAGTGTTGGCAATGAATCCACCCACTCTCCACAGGGAATAAATCTGT
CTCTTAAATGCAAAGAATGTTTCCATGGCCTCTGGATGCAAATACACAGAGCTCTGGGGTC
AGAGCAAGGATGGGGAGAGACCACGAGTGAAAAAGCAGCTACACACATTCACCTAAT
TCCATCTGAGGGCAAGAAAAAAGCAGCTGTT

13711.1

13711.2

TGAGACGGACCACTGGCCTGGTCCCCCCTCATKTGCTGTCGTAGGACCTGACATGAAACGC AGATCTAGTGGCAGAGGAAGATGATGAGGAACTTCTGAGACGTCGGCAGCTTCAAGAA GAGCAATTAATGAAGCTTAACTCAGGCCTGGGACAGTTGATCTTGAAAGAAGAAGATGAGA AAAGAGAGCCGGGGAAAGGTCATCTCTGTTAGCCAGTCGCTACGATTCTCCCATCAACTCAG CTTCACATATTCCATCATCTAAAACTGCATCTCTCCCTGGCTATGGAAGAAATGGGCTTCA CCGGCCTGTTTCTACCGACTTCGCTCAGTATAACAGCTATGGGGATGTCAGCGGGGGGAGTG CGAGATTACCAGACACTTCCAGATGGCCACATGCCTGCAATGAGAATGGACCGAGGAGTG TCTATGCCCAACATGTTGGAACCAAAGATATTTCCATATGAAATGCTCATGGTGACCAACA GAGGGGCCGAAACCAAATCTCAGAGAGGTGGACCAACA

13713.1&2

TCACTITATTTTCTTGTATAAAAACCCTATGTTGTAGCCACAGCTGGAGCCTGAGTCCGCT GCACGGAGACTCTGGTGTGGGTCTTGACGAGGTGGTCAGTGAACTCCTGATAGGGAGACT TGGTGAATACAGTCTCCTTCCAGAGGTCGGGGGGTCAGGTAGCTGTAGGTCTTAGAAATGGC ATCAAAGGTGGCCTTGGCGAAGTTGCCCAGGGTGGCAGTGCAGCCCCGGGCTGAGGTGTA

13715.4

CTGGAATATAGACCCGTGATCGACAAAACTTTGAACGAGGCTGACTGTGCCACCGTCCCGC CAGCCATTCGCTCCTACTGATGAGACAAGATGTGGTGATGACAGAATCAGCTTTTGTAATT ATGTATAATAGCTCATGCATGTGTCCATGTCATAACTGTCTTCATACGCTTCTGCACTCTGG GGAAGAAGGAGTACATTGAAGGGAGATTGGCACCTAGTGGCTGGGAGCTTGCCAGGAACC CAGTGGCCAGGGAGCGTGGCACTTACCTTTGTCCCTTGCTTCATTCTTGTGAGATGATAAA

13-1-132

TGAATGGGGAGGAGCTGACCCAGGAAATGGAGCTTGNGGAGACCAGGCCTGCAGGGGAT
GGAACCTTCCAGAAGTGGGCATCTGTGGTGGTGCCTCTTGGGAAGGAGCAGAAGTACACA
TGCCATGTGGAACATGAGGGGCTGCCTGAGCCCCTCACCCTGAGATGGGGCAAGGAGGAG
CCTCCTTCATCCACCAAGACTAACACAGTAATCATTGCTGTTCCGGTTGTCCTTGGAGCTGT
GGTCATCCTTGGAGCTGTGATGGCTTTTGTGATGAAGAGGAGGAGAACACAGGTGGAAA
AGGAGGGGACTATGCTCTGGCTCCAGGCTCCCAGAGCTCTGATATGTCTCTCCCAGATTGT
TGTGACATCCAGAGACCTCAGTTCTCTTTAGTCAAGTGTTTCACACATCTCC
GGCTCAAAGTGAAGAACTGTGGAGCCCAGTCCACCCCTGCACACCAGGACCCTATCCCTG
CACTGCCCTGTGTTCCCTTCCACAGCCAACCTTGCTGCACACCAGGACCCTATCCCTG
CTGCAGCCTGTCCAGGCTCACAGCCAACCTTGCTCCACACCAGGACCTATCCCTG
CTGCAGCCTGTCAGCTCCATGCTACCCTGACCTTCCACCCCTGCACACTTCCACACTGAGAATA
ATAATTGAATGTGGGTGGCTGGAGAGATGGCTCAGCGCTGACTGCTCCACACTGAGAATA
GAGTTCAAATCCCAGCAACCATGGTGGCTCACACCATCTGTAATGCGCTCTAAAACCT

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13719.1&2

13721.1

13721.2

13723.1

13723.2

13725.1

13725.2

13726.1&2

FIG. 150

13727.1

13727.2

ACCTAGACAGAAGGTGGGTGAGGGAGGACTGGTAGGAGGCTGAGGCAATTCCTTGGTAGT TITGTCCTGAAACCCTACTGGAGAAGTCAGCATGAGGCACCTACTGAGAGAAAGTGCCCAGA AACTGCTGACTGCATCTGTTAAGAGTTAACAGTAAAGAGGTAGAAGTGTGTTTCTGAATCA GAGTGGAAGCGTCCAAAGGGTCCCACAGTGGAGGTCCCTGAGCTACCTCCCTTCCGTGAGT GGGAAGAGTGAAGCCATGAAGAACTGAGATGAAGCAAGGATGGGGTTCCTGGGCTCCA GGCAAGGGCTGTGCTCTTGCAGCAGGGAGCCCCACGAGTCAGAAGAAAAAGAACTAATCA TITGTTGCAAGAAAACCTTGCCCGGATACTAGCGGAAAACTGGAGGCGGNGGTGGGGGCAC AGGAAAGTGGAAGTGATTGATGGAGAGAAAAGTGAAGTGAAGTGAAGTGAAGTGAAGTGAAGTCACACTGGAGGCGGAGTCCAC TTGTAAAGTG

13728.1&2

13731.1&2

TGTGCCAGTCTACAGGCCTATCAGCAGCGACTCCTTCAGCAACAGATGGGGTCCCCTGTTC
AGCCCAACCCCATGAGCCCCCAGCAGCATATGCTCCCAAATCAGGCCCAGTCCCCACACCT
ACAAGGCCAGCAGATCCCTAATTCTCTCTCCAATCAAGTGCGCTCTCCCCAGCCTGTCCCTT
CTCCACGGCCACAGTCCCAGCCCCCCACTCCAGTCCTTCCCCAAGGATGCAGCCTCAGCC
TTCTCCACACCACGTTTCCCCACAGACAAGTTCCCCCACATCCTGGACTGGTAGTTGCCCAG
GCCAACCCCATGGAACAAGGGCATTTTGCCCAGCC

13734.1&2

13736.2

13-44.2-13696.2

13746.1&2-13720.1&2

FIG. 15Q

14347.1

CAGATTITTATITIGCAGTCGTCACTGGGGCCGTTTCTTGCTGCTTATTTGTCTGCTAGCCTG
CTCTTCCAGCTGCATGGCCAGGCGCAAGGCCTTGATGACATCTCGCAGGGCTGAGAAATGC
TTGGCTTGCTGGGCCAGAGCAGATTCCGCTTTGTTCACAAAGGTCTCCAGGTCATAGTCTG
GCTGCTCGGTCATCTCAGAGAGCTCAAGCCAGTCTGGTCCTTGCTGTATGATCTCCTTGAG
CTCTTCCATAGCCTTCTCCTCCAGCTCCCTGATCTGAGTCATGGCTTCGTTAAAGCTGGACA
TCTGGGAAGACAGTTCCTCCTTCCTTGGATAAATTGCCTGGAATCAGCGCCCCGTTAGA
GCAGGCTTCCATCTCTTTCCATTTGAATCAACTGCTCTCCACTGGGCCCACTGTGGG
GGCTCAGCTCCTTGACCCTGCATATCTTAAGGGTGTTTAAAGGATATTCACAGGAGCT
TATGCCTGGT

14347.2

CTCCTCTTGGTACATGAACCCAAGTTGAAAGTGGACTTAACAAAGTATCTGGAGAACCAA
GCATTCTGCTTTGACTTTGATGAAACAGCTTCGAATGAAGTTGTCTACAGGTTCAC
AGCAAGGCCACTGGTACAGACAATCTTTGAAGGTGGAAAAGCAACTTGTTTTGCATATGG
CCAGACAGGAAGTGGCAAGACACATACTATGGGCGGAGACCTCTCTGGGAAAGCCCAGAA
TGCATCCAAAGGGATCTATGCCATGGCCTTCCGGGACGTCTTCTTCTGAAGAATCAACCCT
GCTACCGGAAGTTGGGCCTGGAAGTCTATGTGACATTCTTCGAGATCTACAATGGGAAGCT
GTTTGACCTGCTCAACAAGAAGGCCAAGCTTGCGCGTGCTGGAAGACGGCAACCACAGG
TGCAAGTGGTGGGGGGCTTGCAGGAACATCTGGTTAACATCGCCANTCAAG

14348.2&14350.1&2

14349.1&2

TTCGTGAAGACCCTGACTGGTAAGACCATCACTCTCGAAGTGGAGCCCGAGTGACACCATT GAGAATGTCAAGGCAAAGATCCAAGACAAGGAAGGCATCCCTCCTGACCAGCAKAGGTTG ATCTTTGCTGGGAAACACCCTGGAAGATGGACGCACCCTGTCTGACTACAACATCCAGAAA GAGTCCACCCTGGACCACCCTGGTGCTCCGGAGGTGGGATGCAAATCTTCGTGAAGACCC TGACTGGTAAGACCCTGGAGAGCCCAGTGACACCATCGAGAATGTCAAGG CAAAGATCCAAGATAAAGGTAGCAGCCCTGGATCAGCAGAGATGTCAAGG AACAGCTGGAAGATCTAAGGAAGGCCATCCCTGATCAGCAGAGGTTGATCTTTGCTGGGAAACAGCTGGGAAGATGTCAAGGTTGGTGAGCACCTTGCACTACAACATCCAGAAAGAGTCCACTCTGC ACTTGGTCCTGCGCTTTGAGGGGGGGGGTGTCTAAGTTTCCCCCTTTTTAAGGTTTCAACAAATTTC

14352.1&2

GCGCGGGTGCGTGGGCCACTGGGTGACCGACTTAGCCTGGCCAGACTCTCAGCACCTGGA
AGCGCCCCGAGAGTGACAGCGTGAGGCTGGGAGGAGGACTTGGCTTGAGCTTGTTAAAC
TCTGCTCTGAGCCTCCTTGTCGCCTGCATTTAGATGGCTCCCGCAAAGAAGGGTGGCGAGA
AGAAAAAGGGCCGTTCTGCCATCAACGAAGTGGTAACCCGAGAATACACCATCAACATTC
ACAAGCGCATCCATGGAGTGGGCTTCAAGAAGCGTGCACCTCGGGCACTCAAAGAGATTC
GGAAATTTGCCATGAAGGAGTGGGAACTCCAGATGTGCGCATTGACACCAGGCTCAACA
AAGCTGTCTGGGCCAAAGGAATAAGGAATGTGCCATACCGAATCCGTGTGCGGCTGTCCA
GAAAACGTAATGAGGATGAAAGTTCACCAAATAAGCTATATACTTTGGTTACCTATGTACC
TGTTACCACTTTCAAAAAATCTACAGACAGTCAATGTGGATGAGAACTAATCGCTGATCGT

14353.1

14353.2

17182.132

FIG. 15S

17183.2

GGTTCACAGCACTGCTTGTTGTTGTTGCCGGCCAGGAATTCCAGGCTCACAAGGCTATCT
TAGCAGCTCGTTCTCCGGTTTTTAGTGCCATGTTTGAACATGAAATGGAGGAGAGCAAAAA
GAATCGAGTTGAAATCAATGATGTGGAGCCTGAAGTTTTTAAGGAAATGATGTGCTTCATT
TACACGGGGAAGGCTCCAAACCTCGACAAAATGGCTGATGATTTGCTGGCAGCTGCTGAC
AAGTATGCCCTGGAGCGCTTTAAAGGTCATGTGTGAGGATGCCCTCTGCAGTAACCTGTCCG
TGGAGAACGCTGCAGAAATTCTCATCCTGGCCGACCTCCACAGTGCAGATCAGTTGAAAA
CTCAGGCAGTGGATTTCATCAACTATCATGCTTCGGATGTCTTGGAGACCTCTTGGG

17186.1&2

TCGTAGCCATTITTCTGCTTCTTTGGAGAATGACGCCACACTGACTGCTCATTGTCGTTGGT TCCATGCCAATTGGTGAAATAGAACCTCATCCGGTAGTGGAGCCGGAGGGACATCTTGTC ATCAACGGTGATGGTGCGATTTGGAGCATACCAGAGCTTGGTGTTCTCGCCATACAGGGCA AAGAGGTTGTGACAAAGAGGAGAGATACGGCATGCCTGTGCAGCCCTGATGCACAGTTCC TCTGCTGTGTACTCTCCACTGCCCAGCCGGAGGGGCTCCCTGTCCGACAGATAGAAGATCA

17187.1&2

17191.1339.1

GGGGGTAGGCTCTTTATTAGACGGTTATTGCTGTACTACAGGGTCAGAGTGCAGTGTAAGC
AGTGTCAGAGGCCCGCGTTCAGCCCAAGAATGTGGATTTTCTCTCCCTATTGATCACAGTG
GGTGGGTTTCTTCAGAAAAAGCCCCAGAGGCAGGGACCAGTGAGCTCCAAGGTTAGAAGTG
GAACTGGAAGGCTTCAGTCACATGCTGCTTCCACGCTTCCAGGCTGGCAGCAAGGAGGA
GATGCCCATGACGTGCCAGGTCTCCCCATCTGACACCAGTGAAGTCTGGTAGGACAGCAG
CCGCACGCCTGCCTGCCAGGAGGCCAATCATGGTAGGCAGCATTGCAGGGTCAGAGGT
CTGAGTCCGGAATAGGAGCAGGGCCAGGTCCCTGCGGAGAGGCACTTCTGGCCTGAAGAC
AGCTCCATTGAGCCCCTGCAGTACAGGYGTAGTGCCTTGGACCAAGCCCACAGCCTGGTA
AGGGGCGCCTGCCAGGGCCACGGCCAGGAGGCA

17192.1&2

TAATTTCTTAGTCGTTTGGAATCCTTAAGCATGCAAAAGCTTTGAACAGAAGGGTTCACAA AGGAACCAGGGTTGTCTTATGGCATCCAGTTAAGCCAGAGCTGGGAATGCCTCTGGGTCAT CCACATCAGGAGCAGAAGCACTTGACTTGTCGGTCCTGCCACGGTTTGGGCGCCCACC ACGCCCACGTCCACCTCGTCCTCCCCTGCCGCCACGTCCTGGGCGGCCAAGGTCTCCAAAA TTGATCTCCAGCTGAGACGTTATATCATTTGCTGGCTTCCGGAAATGATGGTCCATAACCG AATETTCAGCATGAGCCTCTTCACTCTTTGATTTATGAAGAACAAATCCCTTCTTCCACTGC CCATCAGCACCTTCATTTGGTTTTCGGATATTAAATTCTACTTTTGCCCGGTCCTTATTTTGA ATAGCCTTCCACTCATCCAAAGTCATCTCTTTTGGACCCTCCTCTTTTACCTCTTCAACTTCA TTCTCCTTATTTTCAGTGTCTGCCACTGGATGATGTTCTTCACCTTCAGGTGTTTCCTCAGTC ACATTTGATTGATCCAAGTCAGTTAATTCGTCTTTGACAGTTCCCCAGTTGTGAGATCCGCT ACCTCCACGTTTGTCCTCGTGCTTCAGGCCAGATCTATCACTTCCACTATGCCTATCAAATT CACGTTTGCCACGAGAATCAAATCCATCTCCTCGGCCCATTCCACGTCCACGGCCCCCTCG ACCTCTTCCAAGACCACCACGACCTCGAATAGGTCGGTCAATAATCGGTCTATCAACTGAA **AATTCGCCTCCTTCACCCTTTTCTTCAAGTGGCTTTTCGAATCTTCGTTCACGAGGTGGTCG** CCTTTCTGGTCTTCTATCAATTATTTTCCCTTCACCCTGAAGTTGTTGATCAGGTCTTCTTCC **AACTCGTGC**

17193

AAGCGGATGGACCTGAGTCAGCCGAATCCTAGCCCCTTCCCTTGGGCCTGCTGTGGTGCTC GACATCAGTGACAGACGGAAGCAGCAGACCATCAAGGCTACGGGAGGCCCGGGGGGGCGCTT GCGAAGATGAAGTTTGGCTGCCTCTCCTTCCGGCAGCCTTATGCTGGCTTTGTCTTAAATG TCGCCGTCCACATTGCTCACAGGGACTGGGAAGGCGATGCCTGTCGGGAGCTGCTGGTGG AGAGACTCGGGATGACTCCTGCTCAGATTCAGGCCTTGCTCAGGAAAGGGGGAAAAGTTTG GTCGAGGAGTGATAGCGGGACTCGTTGACATTGGGGGAAACTTTGCAATGCCCCGAAGACT TAACTCCCGATGAGGTTGTGGAACTAGAAAATCAAGCTGCACTGACCAACCTGAAGCAGA AGTACCTGACTGTGATTTCAAACCCCAGGTGGTTACTGGAGCCCATACCT.\GGAAAGGAG GCAAGGATGTATTCCAGGTAGACATGCCAGAGCACCTGATCCCTTTGGGGCATGAAGTGT GACAAGTGTGGGCTCCTGAAAGGAATGTTCCRGAGAAACCAGCTAAATCATGGCACCTTC AATTTGCCATCGTGACGCAGACCTGTATAAATTAGGTTAAAGATGAATTTCCACTGCTTTG GAGAGTCCCACCACTAAGCACTGTGCATGTAAACAGGTTCCTTTGCTCAGATGAAGGAA GTAGGGGGTGGGGCTTTCCTTGTGTGATGCCTCCTTAGGCACACAGGCAATGTCTCAAGTA CTTTGACCTTAGGGTAGAAGGCAAAGCTGCCAGTAAATGTCTCAGCATTGCTGCTAATTTT GGTCCTGCTAGTTTCTGGATTGTACAAATAAATGTGTTGTAGATGA

FIG. 15U

TCGAGCGGCCGCCGGGCAGGTGTCGGAGTCCAGCACGGGAGGCGTGGTCTTGTAGTTGT
TCTCCGGCTGCCATTGCTCTCCCACTCCACGGCGATGTCGCTGGGATAGAAGCCTTTGAC
CAGGCAGGTCAGGCTGACCTGGTTCTTGGTCATCTCCCCGGGATGGGGGCAGGGTGTAC
ACCTGTGGTTCTCGGGGCTGCCCTTTGGCTTTGGAGATGGTTTTCTCGATGGGGGCTGGGA
GGGCTTTGTTGGAGACCTTGCACTTGTACTCCTTGCCATTCAACCAGTCCTGGTGCANGAC
GGTGAGGACGCTNACCACACGGTACGNGCTGGTGTACTGCTCCCCGCGGCTTTGTCTTG
GCATTATGCACCTCCACGCCGTCCACGTACCAATTGAACTTGACCTCAGGGTCTTCGTGGC
TCACGTCCACCACGCATGTAACCTCAAANCTCGGNCGCGANCACGC

16443.2.edit

16444.2.edit

16445.1.edit

FIG. 15V

16445.2.edit

16-4-46.1.edit

TCGAGCGGCCCGGGCAGGTCCTCCTCAGAGCGGTAGCTGTTCTTATTGCCCCGGCAGC CTCCATAGATNAAGTTATTGCANGAGTTCCTCTCCACGTCAAAGTACCAGCGTGGGAAGG ATGCACGGCAAGGCCCAGTGACTGCGTTGGCGGTGCAGTATTCTTCATAGTTGAACATATC GCTGGAGTGGACTTCAGAATCCTGCCTTCTGGGAGCACTTGGGACAGAGGAATCCGCTGC ATTCCTGCTGGTGGACCTCGGCCGCGACCACGCT

16446.2.edit

AGCGTGGTCGCGGCCGAGGTCCACCAGCAGGAATGCAGCGGATTCCTCTGTCCCAAGTGC
TCCCAGAAGGCAGGATTCTGAAGACCACTCCAGCGATATGTTCAACTATGAAGAATACTG
CACCGCCAACGCAGTCACTGGGCCTTGCCGTGCATCCTTCCCACGCTGGTACTTTGACGTG
GAGAGGAACTCCTGCAATAACTTCATCTATGGAGGCTGCCGGGGCAATAAGAACAGCTAC
CGCTCTGAGGAGGACCTGCCCGGGCGGCGCCGCTCGA

16447.1.edit

FIG. 15W

16447.2.edit

16449.1.edit

AGCGTGGTCGCGGCCGAGGTCCTGTCAGAGTGGCACTGGTAGAAGNTCCAGGAACCCTGA
ACTGTAAGGGTTCTTCATCAGTGCCAACAGGATGACATGAAATGATGTACTCAGAAGTGTC
CTGNAATGGGGCCCATGANATGGTTGNCTGAGAGAGAGCTTCTTGTCCTACATTCGGCGG
GTATGGTCTTGGCCTATGCCTTATGGGGGGTGGCCGTTGNGGGCGGTGNGGTCCGCCTAAAA
CCATGTTCCTCAAAGATCATTTGTTGCCCAACACTGGGTTGCTGACCANAAGTGCCAGGAA
GCTGAATACCATTTCCAGTGTCATACCCAGGGTGACGAAAGGGGTCTTTTGAACTGT
GGAAGGAACATCCAAGATCTCTGNTCCATGAAGATTGGGGTGTGGAAGGGTTACCAGTTG
GGGAAGCTCGCTGTCTTTTTCCTTCCAATCANGGGCTCGCTCTTCTGAATATTCTTCAGGGC
AATGACATAAATTGTATATTCGGTTCCCGGTTCCAGGCCAG

16450.1.edit

16450.2.edit

AGCGTGGTCGCGGGCGAGGTCCTGTCAGAGTGGCACTGGTAGAAGTTCCAGGAACCCTGA
ACTGTAAGGGTTCTTCATCAGTGCCAACAGGATGACATGAAATGATGTACTCAGAAGTGTC
CTGGAATGGGGCCCATGAGATGGT.GTCTGAGAGAGAGAGCTTCTTGTCCTACATTCGGCGGG
TATGGTCTTGGCCTATGCCTTATGGGGGTGGCCGTTGTGGGCGGTGTGGTCCGCCTAAAAC
CATGTTCCTCAAAGATCATTTGTTGCCCAACACTGGGTTGCTGACCAGAAGTGCCAGGAAG
CTGAATACCATTTCCAGTGTCATACCCAGGGTGGGTGACGAAAGGGGTCTTTTGAACTGTG
GAAGGAACATCCAAGATCTCTGGTCCATGAAGATTGGGGTGTGGAAGGGTTACCAGTTGG
GGAAGCTCGTCTTTTTCCTTCCAATCANGGGCTCGCTCTTCTGATTATTCTTCAGGGC
AATGACATAAATTGTATATTCGCNTCCCGGGTNCAGCCAATAATAATAACCCTCTGTGACA
CCANGGCGGGGCCGAAGGANCACT

AGCGTGGTCGCGGCCGAGGTCCTCACCAGAGGTACCACCTACAACATCATAGTGGAGGCA CTGAAAGACCAGCAGAGGCATAAGGTTCGGGAAGAGGTTGTTACCGTGGGCAACTCTGTC AACGAAGGCTTGAACCAACCTACGGATGACTCGTGCTTTGACCCCTACACAGTTTCCCATT ATGCCGTTGGAGATGAGTGGGAACGAATGTCTGAATCAGGCTTTAAACTGTTGTGCCAGTG CTTANGCTTTGGAAGTGGTCATTTCAGATGTGATTCATCTAGATGGTGCCATGACAATGGT GTGAACTACAAGATTGGAGAGAAGTGGGACCGTCAGGGGAGAAAATGGACCTGCCCGGGC

16451.2.edit

16452.1.edit

AGCGTGGCCGCGGCCGAGGTCCATTGGCTGGAACGGCATCAACTTGGAAGCCAGTGATCG
TCTCAGCCTTGGTTCTCCAGCTAATGGTGATGGNGGTCTCAGTAGCATCTGTCACACGAGC
CCTTCTTGGTGGGCTGACATTCTCCAGAGTGGTGACAACACCCTTGAGCTGGTCTGCTTGTC
AAAGTGTCCTTAAGA 3CATAGACACTCACTTCATATTTGGCGNCCACCATAAGTCCTGATA
CAACCACGGAATGACCTGTCAGGAAC

16452.2.edit

FIG. 15Y

16453.2.edit

16454.1.edit

AGCGTGGNTGCGGACGACGCCCACAAAGCCATTGTATGTAGTTTTANTTCAGCTGCAAAN AATACCNCCAGCATCCACCTTACTAACCAGCATATGCAGACA

16454.2.edit

TCGAGCGGTCGCCCGGGCAGGTTTGGGCCGGATAGCACCGGGCATATTTTGGAATGGATGA GGTCTGGCACCCTGAGCAGCCCAGCGACGACTTGGTCTTAGTTGAGCAATTTGGCTAGGA GGATAGTATGCAGCACGGTTCTGAGTCTGTGGGATAGCTGCCATGAAGNAACCTGAAGGA GGCGCTGGCTGGTANGGGTTGATTACAGGGCTTGGGAACAGCTCGTACACTTGCCATTCTCT GCATATACTGGNTAGTGAGGCGAGCCTGGCGCTCTTCTTTGCGCTGAGCTAAAGCTACATA CAATGGCTTTGNGGACCTCGGCCGCGACCACGCTT

16455.2.edit

AGCGTGGTTTGCGGCCGAGGTCCTCACCANAGGTGCCACCTACAACATCATAGTGGAGGC ACTGAAAGACCAGCAGAGGCATAAGGTTCGGGAAGAGGTTGTTACCGTGGGCAACTCTGT CAACGAAGGCTTGAACCAACCTACGGATGACTCGTGCTTTGACCCCTACACAGNTTCCCAT TATGCCGTTGGAGATGAGTGGGAACGAATGTCTGAATCAGGCTTTAAACTGTTGTGCCAGT GCTTANGCTTTGGAAGTGGTCATTTCAGATGTGATCATCTANATGGTGTCATGACAATGG TGNGAACTACAAGATTGGAGAGAAGTGGNACCGTCAGGGGANAAAATGGACCTGCCCGG GCGGCNCGCTCGA

16456.1.edit

16456.2.edir

TCGAGCGGCCGCGGGCAGGTCCAATTGAAACAAACAGTTCTGAGACCGTTCTTCCACCA CTGATTAAGAGTGGCGNGGCGGGTATTAGGGATAATATTCATTTAGCCTTCTGAGCTTTCT GGGCAGACTTGGTGACCTTGCCAGCTCCAGCAGCCTTCTGGTCCACTGCTTTGATGACACC CACCGCAACTGTCTGTCTCATATCACGAACAGCAAAGCGACCCAAAGGTGGATAGTCTGA GAAGCTCTCAACACACATGGGCTTGCCAGGAACCATATCAACAATGGGCAGCATCACCAG ACTTCAAGAATTTAAGGGCCATCTTCCAGCTTTTTACCAGAACGGCGATCAATCTTTTCCTT CAGCTCAGCAAACTTGCATGCAATGTGAGCCG

FIG. 15.4A

16459,2.edit

16460.1.edit

16460.2.edit

FIG. 15BB

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AGCGTGGTCGCGGCCGAGGTCCACATCGGCAGGGTCGGAGCCCTGGCCGCCATACTCGAA CTGGAATCCATCGGTCATGCTCTCGCCGAACCAGACATGCCTCTTGTCCTTGGGGTTCTTGC TGATGTACCAGTTCTTCTGGGCCACACTGGGCTGAGTGGGGTACACGCAGGTCTCACCAGT CTCCATGTTGCAGAAGACTTTGATGGCATCCAGGNTGCAACCTTGGTTGGGGTCAATCCAG TACTCTCCACTCTTCCAGCCAGAGTGGCACATCTTGAGGTCACGGCAGGTGCGGNCGGGGG NTTTTGCGGCTGCCCTCTGGNCTTCGGNTGTNCTCNATCTGCTGGCTCA

16461.2.edit

16463.1.edit

AGCGTGGNNGCGGCCGAGGTATAAATATCCAGNCCATATCCTCCCTCCACACGCTGANAGATGAAGCTGTNCAAAGATCTCAGGGTGGANAAAACCAT

16463.2.edit

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FIG. 15CC

CGAGCGGCGACCGGGCAGGTNCAGACTCCAATCCANANAACCATCAAGCCAGATGTCAG
AAGCTACACCATCACAGGTTTACAACCAGGCACTGACTACAAGANCTACCTGCACACCTTG
AATGACAATGCTCGGAGCTCCCCTGTGGTCATCGACGCCTCCACTGCCATTGATGCACCAT
CCAACCTGCGTTTCCTGGCCACCACACCCCAATTCCTTGCTGGTATCATGGCAGCCGCCACG
TGCCAGGATTACCGGTACATCATCNAGTATGANAAGCCTGGGCCTCCTCCCAGAGAAGNG
GTCCCTCGGCCCCGCCCTGNTGTCCCANAGGNTACTATTACTGNGCCNGCAACCGGCAACC
GATATCNATTTTGNCATTGGCCTTCAACAATAATTA

16464.2.edit

16465.1.edit

AGCGTGGNCGCGGCCGAGGTGCAGCGCGGGCTGTGCCACCTTCTGCTCTCTCCCCAACGAT AAGGAGGGTNCCTGCCCCCAGGAGAACATTAACTNTCCCCAGCTCGGCCTCTGCCGG

16465.2.adit

TCGAGCGGCCGGGCAGGTTTTTTCGTGAAAGTGGNTACTTTATTGGNTGGGAAAG GGAGAAGCTGTGGTCAGCCCAAGAGGGAATACAGAGNCCCGAAAAAAGGGGAGGGCAGGT GGGCTGGAACCAGACGCCAGGGCAGAAACTTTCTCTCCTCACTGCTCAGCCTGGTG GTGGCTGGAGCTCANAAATTGGGAGTGACACAGGACACCTTCCCACAGCCATTGCGGCGG CATTTCATCTGGCCAGGACACTGGCTGTCCACCTGGCACTGGTCCCGACAGAAGCCCGAGC TGGGGAAAGTTAATGTTCACCTGGGGGCAGGAACCCTCCTTATCATTGNGCAGAGAGCAG AAGGTGGCACAGCCCGCGCTGCACCTCGCGCCCCCCT

16466.2.edir

TCGAGCGGCCGCCCGGGCAGGTCCACCATAAGTCCTGATACAACCACGGATGAGCTGTCA GGAGCAAGGTTGATTTCTTTCATTGGTCCGGNCTTCTCCTTGGGGGNCACCCGCACTCGAT ATCCAGTGAGCTGAACATTGGGTGGCGTCCACTGGGCGCTCAGGCT

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TCGAGCGGTTCGCCCGGGCAGGTCCACACACACACACATTCCTTGCTGGTATCATGGCAGCCGCACGTGCCAGGGTTACCAGGCTACATCATCAAGTATGAGAAGCCTGGGTCTCCTCCCAGAGAAGCGGTCCCTCGGCCCCGGGTGTCACAGAGGGCTACTATTACTGGCCTGGAACCGGGAACCGGGAACCGAATTTATGTCATTGNCCTGAAGAATAATCANNAANAGCGANCCCCTGATTGGAAGGA

FIG. 15DD

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TCGAGCGGCCGCGGGCAGGTCTCCCTTCTTGCGGCCCAGGGGCAGCGCATAGTGGGAC
TCGTACCACTGTCGGTACGGTGTGCTGTGGATGAGCACGATGCAATTCTTCACCAGGGTCT
TGGTACGAACCACTCTGAGCCCCAGGAGAAATTCCCCCACGTCCAACCTCGATGATCCTTGTTTTACG
AGTACAACACTCTGAGCCCCAGGAGAAATTCCCCCACGTCCAACCTCAGGGCACGGTATTTC
TTGTTACCTCCCCGCACACGGACTGTGTGGATGCGCCGGGGCCCAAGCTGACTCCTGAGGA
AGAAGAGTTTTAAACAAAAAAACGATCTCAAAAAAATTCAGAAGAAATATGATGAAAGGA
AAAAGAATGCCAAAATCAGCAGTCTCCTGGAGGAGCAGTTCCAGCAGGGCAAGCTTCTTG
CGTGCATCGCTTCAAGGCCGGGACAGTGTGACCGAGCAGATGGCTATGTGCTAGAGGGCA
AAGAAGTGGAGTTCTATCTTAAGAAAATCAGGGCCCAGAATGGTGNGTCTTCAACTAATC
CAAAGGGGAAGTTTCAGACCAGTGCAATCAGCAAAAACATTGATACTGNTGGCCAAATTTA
TTGGTGCAGGGCTTGCACANTANGANNGGCTGGGTCTTGGGGCTTTGGATTGGNACAAGCT
TTGGTGCAGGGCTTTCTTTGGTTTTGCCAAAAAACCTTTGTTGAAGAAGANACCTNGGGCGGA
CCCCTTAACCGATTCCACNCCNGGNGGCGTTCTANGGNCCCNCTTG

FIG. 15EE

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AGCGTGGTCGCGGCCGAGGTCTGCTGCTTCAGCGAAGGGTTTCTGGCATAACCAATGATA
AGGCTGCCAĀAGACTGTTCCAATACCAGCACCAGAACCAGCCACTCCTACTGTTGCAGCAC
CTGCACCAATAAATTTGGCAGCAGTATCAATGTCTCTGCTGATTGCACTGGTCTGAAACTC
CCTTTGGATTAGCTGAGACACACCATTCTGGGCCCTGATTTTCCTAAGATAGAACTCCAAC
TCTTTGCCTCTAGCACATAGCCATCTGCTCGGTCACACTGTCCCGGCCTTGAAGCGATGC
ACGCAAGAAGCTTGCCCTGCTGGAACTGCTCCTCCAGGAGACTGCTGATTTTGGCATTCTT
TTTCCTTTCATCATATTTCTTCTGAATTTTTTTAGATCGTTTTTTGTTTAAAATCTCTTCTCC
TCAGGAGTCAGCTTGGCCCCCGCCGCATCCACACAGTCCGTGTGCGGGGAGGTAACAAGA
AATACCGTGCCCTGAGGTTGGACGTGGGGGAATTTCTCCTGGGGCTCAGAGTGGTGTACTCG
TAAAACAAGGATCATCGATGGTGNCTACAATGCATCTAATAACGAGCTGGGTCGGACCCA
AAGAACCTGGNGAANAAATGGATCGNCTCATCGACAGGACACCGTACCCGACAGGGGNA
CGAAAGCCCAATTNTGGAAAAAATCCATCACACTGGNGGCCNGTCGAGCATGCATNTAN
AGGGGCCCATTCCCCCTNANN

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TCGAGCGGCCGCCGGGCAGGTCCCCAACCAAGGCTGCAACCTGGATGCCATCAAAGTCT TCTGCAACATGGAGACTGGTGAGACCTGCGTGTACCCCACTCAGCCCAGTGTGGCCCAGA AGAACTGGTACATCAGCAAGAACCCCCAAGGACAAGAGGCATGTCTGGTTCGGCGAGAGCA TGACCGATGGATTCCAGTTCGAGTATGGCGGCCAGGGCTCCGACCCTGCCGATGTGGACCT CGGCCGCGACCACGCT

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FIG. 15FF

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AGCGTGGTTNGCGGCCGAGGTCTGGGGCAGGGGCACCAACACGTCCTCTCACCAGGAAGCCCACGGGCTCCACGGGCCACCAGGTTCACCAGGACCCACGGGCCACCAGGTTCACCCTTCACACCAGGGCCACCAGGGTTCACCCTTCACACCAGGAGCACCAGGTCCCCTACATGCCTTTGAAGCCAGGAAGTCCAGGAGTTCCAGGGAAACCACCGAGCACCCTGTGGTCCAACAACTCCTCTCACCAGGTCGTCCCAGGGTTTTCCAGGGTGACCATCTTCACCAGCCTTGCCAGGAGCACCAGGCTTGCCAGGAGCACCAGCCTTGCCAGGAGCACCAGCCTTGCCAGGAGCACCAGCCTTGCCAGGACCAGCCTTGCCAGGACCAGCCTTGCCAGGACCAGCCTGCCGGGCGGCGCGCCGCTCGA

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AGCGTGGTCGCGGCCGAGGTCCTCACCAGAGGTGCCACCTACAACATCATAGTGGAGGCA
CTGAAAGACCAGCAGAGGCATAAGGTTCGGGAAGAGGTTGTTACCGTGGGCAACTCTGTC
ÆACGAAGGCTTGAACCAACCTACGGATGACTCGTGCTTTGACCCCTACACAGTTTCCCATT
ATGCCGTTGGAGATGAGTGGGAACGAATGTCTGAATCAGGCTTTAAACTGTTGTGCCAGTG
CTTAGGCTTTGGAAGTGGTCATTTCAAGATGTGATCATCTAGATGGTGCCATGACAATGG
TGTGAACTACAAGATTGGAGAGAAGTGGGGACCGTCAGGGAGAAAATGGACCTGCCCGGG
CCGGCCGCTCGA

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TCGAGCGNNCGCCCGGGCAGGTCCAGTAGTGCCTTCGGGACTGGGTTCACCCCCAGGTCTG
CGGCAGTTGTCACAGCGCCAGCCCCGCTGGCCTCCAAAGCATGTGCAGGAGCAAATGGCA
CCGAGATATTCCTTCTGCCACTGTTCTCCTACGTGGTATGTCTTCCCATCATCGTAACACGT
TGCCTCATGAGGGTCACACTTGAATTCTCCTTTTCCGTTCCCAAGACATGTGCAGCTCATTT
GGCTGGCTCTATAGTTTGGGGAAAGTTTGTTGAAACTGTGCCACTGACCTTTACTTCCTCCT
TCTCTACTGGAGCTTTCGTACCTTCCACTTCTGCTGTTGGTAAAATGGTGGATCTTCTATCA
ATTTCATTGACAGTACCCACTTCTCCCAAACATCCAGGGAAATAGTGATTTCAGAGCGATT
AGGAGAACCAAATTATGGGGCAGAAATAAGGGGCTTTTCCACAGGTTTTCCTTTGGAGGA
AGATTTCAGTGGTGACTTTAAAAGAATACTCAACAGTGTCTTCATCCCCATAGCAAAAGAA
GAAACNGTAAATGATGGAANGCTTCTGGAGATGCCNNCATTTAAGGGACNCCCAGAACTT
CACCATCTACAGGACCTACTTCAGTTTACANNAAGNCACATANTCTGACTCANAAAGGAC
CACCATCTACAGGACCTACTTCAGTTTACANNAAGNCACATANTCTGACTCANAAAGGAC
CCAAGTAGCNCCATGGNCAGCACTTTNAGCCTTTCCCCTTGGGGGAAAANNTTACNTTCTTAA
ANCCTNGGCCNNGACCCCCTTAAGNCCAAATTNTGGAAAAANTTCCNTNCNCTGGGGGGC
NGTTCNACATGCNTTTNAAGGGCCCCAATTNCCCCCNT

25_16481.edit

TCGAGCGGCCGCCCGGGCAGGTGTCGGAGTCCAGCACGGGAGGCGTGGTCTTGTAGTTGT
TCTCCGGCTGCCATTGCTCTCCCACTCCACGGCGATGTCGCTGGGATAGAAGCCTTTGAC
CAGGCAGGTCAGGCTGACCTGGGTCTTGGCTCATCTCCTCCCGGGATGGGGGCAGGGTGTAC
ACCTGTGGTTCTCGGGGCTGCCCTTTGGCTTTTGGAGATGGTTTTCTCGATGGGGGCTGGGA
GGGCTTTGTTGGAGACCTTGCACTTGTACTCCTTGCCATTCAGCCAGTCCTGGTGCAGGAC
GGTGAGGACGCTGACCACACGGGTACGTGTTGTACTGCTCCTCCCGCGGCTTTGTCTTG
GCATTATGCACCTCCACGCCGTCCACGTACCAGTTGAACTTGACCTCAGGGTCTTCGTGGC
TCACGTCCACCACCACGCATGTAACCTCAGACCTCGGCCGCGACCACGCT

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TCGAGCGGCCGCGGGCAGGTTGAATGGCTCCTCGCTGACCACCCCGGTGCTGGTGGTGG GTACAGAGCTCCGATGGGTGAAACCATTGACATAGAGACTGTCCCTGTCCAGGGTGTAGG GGCCCAGCTCAGTGATGCCGTGGGTCAGCTGGCTCAGCTTCCAGTACAGCCGCTCTCTGTC CAGTCCAGGGCTTTTGGGGTCAGGACGATGCAGCAGCATCCACTCTGGTGGCTGC CCCATCCTTCTCAGGCCTGAGCAAGGTCAGTCTGCAACCAGAGTACAGAGAGCTGACACT GGTGTTCTTGAACAAGGGCATAAGCAGACCCTGAAGGACACCTCGGCCGCCGACCACGCT

FIG. 15JJ

23_16482.edit

AGCGTGGTCGCGGCCGAGGTGTCCTTCAGGGTCTGCTTATGCCCTTGTTCAAGAACACCAG TGTCAGCTCTCTGTACTCTGGTTGCAGACTGACCTTGCTCAGGCCTGAGAAGGATGGGGCA GCCACCAGAGTGGATGCTGTCTGCACCCATCGTCCTGACCCCAAAAGCCCCTGGACTGGACA GAGAGCGGCTGTACTGGAAGCTGAGCCAGCTGACCCACGGCATCACTGAGCTGGGCCCCT ACACCCTGGACAGGGACAGTCTCTATGTCAATGGTTTCACCCATCGGAGCTCTGTACCCAC CACCAGCACCGGGGTGGTCAGCGAGGAGCCATTCAACCTGCCCGGGCGGCCGCTCGA

29_16483.edit

AGCGTGGTCGCGGCCGAGGŤCCTGTCAGAGTGGCACTGGTAGAAGTTCCAGGAACCCTGA
ACTGTAAGGGTTCTTCATCAGTGCCAACAGGATGACATGAAATGATGTACTCAGAAGTGTC
CTGGAATGGGGCCCATGAGATGGTTGTCTGAGAGAGAGGCTTCTTGTCCTACATTCGGCGGG
TATGGTCTTGGCCTATGCCTTATGGGGGGTGGCCGTTGTGGGCGGTTGGTCCGCCTAAAAC
CATGTTCCTCAAAGATCATTTGTTGCCCAACACTGGGTTGCTGACCAGAAGTGCCAGGAAG
CTGAATACCATTTCCAGTGTCATACCCAGGGTTGGTGACGAAAGGGGTCTTTTGAACTGTG
GAAGGAACATCCAAGATCTCTGGTCCATGAAGATTGGGGTGTGGAAGGGTTACCAGTTGG
GGAAGCTCGTCTTTTTCCTTCCAATCAGGGGCTCGCTCTTCTGATTATTCTTCAGGGC
AATGACATAAATTGTATATTCGGTCCCGGTTCCAGGCCAGTAATAGTAGCCTCTTTGACAC
CAGGGCGGGGCCGAGGGACCCTTCTNTTGGAAGAGACCAGCTTCTCATACTTGATGATGA
GNCCGGTAATCCTGGCACGTGGNGGTTGCATGATNCCACCAAGGAAATNGGNGGGGGNG
GACCTGCCCGGCGGCCGTTCNAAAGCCCAATTCCACACACTTGGNGGCCGTACTATGGATC
CCACTCNGTCCAACTTGGNGGAATATGGCATAACTTTT

31_16484.edit

TCGAGCGGCCGGCCGGGCAGGTCCTTGACCTTTTCAGCAAGTGGGAAGGTGTAATCCGTCT CCACAGACAAGGCCAGGACTCGTTTGTACCGGTTGATGATAGAATGGGGTACTGATGCAA CAGTTGGGTAGCCAATCTGCAGACAGACACTGGCCAACATTGCGGACACCCTCCAGGAAGC GAGAATGCAGAGTTTCCTCTGTGATATCAAGCACTTCAGGGTTGTAGATGCTGCCATTGTC GAACACCTGCTGGATGACCAGCCCAAAGGAGAGGGGAGATGTTGAGCATGTTCAGCAG CGTGGCTTCGCTGGCTCCCACTTTGTCTCCAGTCTTGATCAGACCTCGGCCGCGACCACGCT

37_16487.edit

AGCQTGGTCGCGGCCGAGGTCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTG
GTGACCGTGCCCTCCAGCAACTTCGGCACCCAGACCTACACCTGCAACGTAGATCACAAGC
CCAGCAACACCCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGACAAAACTCACACAT
GCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCGCAT
CCCCCTTCCAAACCTGCCGGGGGGGCCGCTCG

38_16487.edit

CGAGCGGCCGCCCGGGCAGGTTTGGAAGGGGGATGCGGGGGAAGAGAGAAGACTGACGGT CCCCCAGGAGTTCAGGTGCTGGGCACGGTGGGCATGTGTGAGTTTTGTCACAAGATTTGG GCTCAACTCTCTTGTCCACCTTGGTGTTGCTGGGCTTGTGATCTACGTTGCAGGTGTAGGTC TGGGTGCCGAAGTTGCTGGAGGGCACGGTCACCACGCTGCTGAGGGAGTAGAGTCCTGAG GACTGTAGGACAGACCTCGGCCGCGACCACGCT

39_16488.edit

NGGNNGGTCCGGNCNGNCAGGACCACTCNTCTTCGAAATA

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AGCGTGGTCGCGGCCGAGGTCCTCACTTGCCTCCTGCAAAGCACCGATAGCTGCGCTCTGGAGCGCAGATCTGTTTTAAAGTCCTGAGCAATTTCTCGCACCAGACGCTGGAAGGGAAGTTTGCGAATCAGAAGTTCAGTGGACTTCTGATAACGTCTAATTTCACGGAGCGCCCACAGTACCAGGACCTGCCCGGGCGGCGCCCCACAGTACC

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FIG. 15LL

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AGCGTGGTCGCGGCCGAGGTCCTCACCAGAGGTGCCACCTACAACATCATAGTGGAGGCA
CTGAAAGACCAGCAGAGGCATAAGGTTCGGGAAGAGGTTGTTACCGTGGCCAACTCTGTC
AACGAAGGCTTGAACCAACCTACGGATGACTCGTGCTTTGACCCCTACACAGTTTCCCATT
ATGCCGTTGGAGATGAGTGGGAACGAATGTCTGAATCAGGCTTTAAACTGTTGTGCCAGTG
CTTAGGCTTTGGAAGTGGTCATTTCAGATGTGATCATCTAGATGGTGCCATGACAATGGT
GTGAACTACAAGATTGGAGAGAAGTGGGACCGTCAGGGAGAAAATGGACCTGCCCGGGC

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TCGAGCGGCCGCGGGCAGGTCCATTTCTCCCCTGACGGTCCCACTTCTCTCCAATCTTGT
AGTTCACACCATTGTCATGGCACCATCTAGATGAATCACATCTGAAATGACCACTTCCAAA
GCCTAAGCACTGGCACAACAGTTTAAAGCCTGATTCAGACATTCGTTCCCACTCATCTCCA
ACGGCATAATGGGAAACTGTGTACGGGTCAAAGCACGAGTCATCCGTAGGTTGCTTCAAG
CCTTCGTTGACAGAGTTGCCCCACTGTAACAACCTCTTCCCGAACCTTATGCCTCTGCTGGTC
TTTCAGTGCCTCCACTATGATGTTGTAGGTGGCACCTCTGGTGAGGACCTCGGCCGCGGACC
ACGCT

59_16498.edit

TCGAGCGGCCGCCGGGCAGGTCCACCATAAGTCCTGATACAACCACGGATGAGCTGTCA
GGAGCAAGGTTGATTTCTTTCATTGGTGCGGTCTTCTCCTTGGGGGTCACCCGCACTCGATA
TCCAGTGAGCTGAACATTGGGTGCAGCACTGGGCGCTCAGGCTTGTGGGTGTGACCTGA
GTGAACTTCAGGTCAGTTGGTGCAGGAATAGTGGTTACTGCAGTCTGAACCAGAGGCTGA
CTCTCTCCGCTTGGATTCTGAGCATAGACACTAACCACATACTCCACTGTGGGCTGCAAGC
CTTCAATAGTCATTTCTGTTTGATCTGGACCTGCAGTTTTAGTTTTTGTTGGTCCTGGTCCAT
TTTTGGGAGTGGTGGTTACTCTGTAACCAGTAACAGGGGAACTTGAAGGCAGCCACTTGAC
ACTAATGCTGTTGTCCTGAACATCGGTCACTTGCATCTTGGGATGGTTTGNCAATTTCTGTTC
GGTAATTAATGGAAATTGGCTTGCTGCTGCTGCGGGGCTGTCTCCACGGCCAGTGACAGCATA
CACAGNGATGGNATNATCAACTCCAAGTTTAAGGCCCTGATGGTAACTTTAAACTTGCTCC
CACAGNGAACTTCCGGACAGGGTATTTCTTCTGGTTTTCCGAAAGNGANCCTGGAATNN
TCTCCTTGGGANCAGAAGGANCNTCCAAAACTTGGGCCGGAACCCCTT

FIG. 15NN

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AGCGTGGTCGCGGCCGAGGTCNAGGA

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FIG. 1500

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TCGAGCGGCCGGGCAGGTCCTCACCAGAGGTGCCACCTACAACATCATAGTGGAGG CACTGAAAGACCAGCAGAGGCATAAGGTTCGGGAAGAGGTTGTTACCGTGGGCAACTCTG TCAACGAAGGCTTGAACCAACCTACGGATGACTCGTGCTTTGACCCCTACACAGTTTCCCA TTATGCCGTTGGAGATGAGTGGGAACGAATGTCTGAATCAGGCTTTAAACTGTTGTGCCAG TGCTTAGGCTTTGGAAGTGGTCATTTCAGATGTGATCATCTAGATGGTGCCATGACAATG GTGTGAACTACAAGATTGGAGAGAAGTGGGACCGTCAGGGAGAAAATGGACCTCGGCCG CGACCACGCT

FIG. 15PP

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16501.edit

16501.2.edit

GAGGACTGGCTCAGCTCCCAGTATAGCCGCTCTCTGTCCAGTCCAGGACCAGTGGGATCAA GGCGGAGGGTGCAGATGGCGTCCACTCCAGTGGCTGCCCCATGTTTCTCAAGTCTGAGCAA AGNCAGTCTGCAGCCAGAGTACAGAGGGCCAACACTGGTGCTCTTGAACAGGGACCTGAG CAGGCCCTGAAGGACCCTCTCCGTGGTGTTTGAACTTCCTGGAGCCAGGGTGCTGCATGTTC TCCTCATACCGCAGGTTGTTGATGGTGAAGTTCAGTGTGAATGGCTCCTCGCTGACCACCC

16502.1.edit

16502.2.edit

FIG. 15QQ

AGCGTGGNCGCGGGCCGAGGTCTGAGGATGTAAACTCTTCCCAGGGGAAGGCTGAAGTGCT
GACCATGGTGCTACTGGGTCCTTCTGAGTCAGATATGTGACTGATGNGAACTGAAGTAGGT
ACTGTAGATGGTGAAGTCTGGGTGTCCCTAAATGCTGCATCTCCAGAGCCTTCCATCATTA
CCGTTTCTTCTTTTGCTATGGGATGAGACACTGTTGAGTATTCTCTAAAGTCACCACTGAAA
TCTTCCTCCAAAGGAAAACCTGTGGAAAAGCCCCTTATTTCTGCCCCATAATTTGGTTCTCC
TAATCNCTCTGAAATCACTATTTCCCTGGAANGTTTGGGAAAAANNGGGCNACCTGNCAN
TGGAAANTGGATANAAAGGATCCCACCATTTTACCCAACNAGCAGAAAGTGGGAANGGTAC
CGAAAAGCTCCAAGTAANAAAAAGGAGGGAAGTAAAGGTCAAGTGGGCACCAGTTTCAA

16503.2.edit

AAGCGGCCGCCGGGCAGGNNCAGNAGTGCCTTCGGGACTGGGNTCACCCCCAGGTCTGC
GGCAGTTGTCACAGCGCCAGCCCCGCTGGCCTCCAAAGCATGTGCAGGAGCAAATGGCAC
CGAGATATTCCTTCTGCCACTGTTCTCCTACGTGGTATGTCTTCCCATCATCGTAACACGTT
GCCTCATGAGGGTCACACTTGAATTCTCCTTTTCCGTTCCCAAGACATGTGCAGCTCATTTG
GCTGGCTCTATAGTTTGGGGAAAGTTTGTTGAAACTGTGCCACTGACCTTTACTTCCTCCTT
CTCTACTGGAGCTTTCCGTACCTTCCACTTCTGCTGNTGGNAAAAAGGGNGGAACNTCTTA
TCAATTTCATTGGACAGTANCCCNCTTTCTNCCCAAAACATNCAAGGGAAAATATTGATTN
CNAGAGCGGATTAAGGAACAACCCNAATTATGGGGGGCCCAGAAATAAAAGGGGGGCTTTTCCA
CAGGTNTTTTCCT

16504.1.edi:

TCGAGCGGCCGGGCAGGTCTGCAGGCTATTGTAAGTGTTCTGAGCACATATGAGAT AACCTGGGCCAAGCTATGATGTTCGATACGTTAGGTGTATTAAATGCACTTTTGACTGCCA TCTCAGTGGATGACAGCCTTCTCACTGACAGCAGAGATCTTCCTCACTGTGCCAGTGGGCA GGAGAAAGAGCATGCTGCGACTGGACCTCGGCCGCGACCACGCT

16504.2.edit

AGCGTGGTCGCGGCCGAGGTCCAGTCGCAGCATGCTCTTTCTCCTGCCCACTGGCACAGTG AGGAAGATCTCTGCTGTCAGTGACAAGGCTGTCATCCACTGAGATGGCAGTCAAAAGTGC ATTTAATACACCTAACGTATCGAACATCATAGCTTGGCCCAGGTTATCTCATATGTGCTCA GAACACTTACAATAGCCTGCAGACCTGCCCGGGCCGCCCCTCGA

FIG. 15RR

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16505.1.edit

CGAGCGGCCGCCCGGGCAGGTCCAGACTCCAATCCAGAGAACCACCAAGCCAGATGTCAG
AAGCTACACCATCACAGGTTTACAACCAGGCACTGACTACAAGATCTACCTGTACACCTTG
AATGACAATGCTCGGAGCTCCCCTGTGGTCATCGACGCCTCCACTGCCATTGATGCACCAT
CCAACCTGCGTTTCCTGGCCACCACACCCAATTCCTTGCTGGTATCATGGCAGCCGCCACG
TGCCAGGATTACCGGCTACATCATCAAGTATGAGAAGCCTGGGTCTCCTCCCAGAGAAGT
GGTCCCTCGGCCCCGCCCTGGTGNCACAGAAGCTACTATTACTGGCCTTGGAACCGGGAACC
GAATATACAATTTATGTCATTGCCCTGAAGAATAATCANAAGAGCGAGCCCCTGATTGGA

16505.2.edit

16506. Ledic

TCGAGCGGCCGGGCAGGTTTCGTGACCGTGACCTCGAGGTGGACACCACCCTCAAG
AGCCTGAGCCAGCAGATCGAGAACATCCGGAGCCCAGAGGGCAGCCGCAAGAACCCCGC
CCGCACCTGCCGTGACCTCAAGATGTGCCACTCTGACTGGAAGAGTGGAGAGTACTGGAT
TGACCCCAACCAAGGCTGCAACCTGGATGCCATCAAAGTCTTCTGCAACATGGAGACTGGT
GAGACCTGCGTGTACCCCCACTCAGCCCAGTGTGGCCCAGAAGAACTGGTACATCAGCAAG
AACCCCAAGGACAAGAAGCATGTCTGGTTCCGGCGAAAGCATGGATTCCAGTTC
GAGTATGGCGGCCAGGGCTCCGACCCTGCCGATTGGACCTCGGCCGCGACCACGCTAAG
CCCGAATTCCAGCACACTGGCGGCCGTTACTAGTGGATCCGAGCTTCGGTACCAAGCTTG
GCGTAATCATGGGNCATAGCTGTTTCCTGNGTGAAAATGGTATTCCGCTTCACAATTTCCC
AC

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16510.1.edit

TCGAGCGGCCGGGCAGGTCCTTGCAGCTCTGCAGTGTCTTCTTCACCATCAGGTGCA
GGGAATAGCTCATGGATTCCATCCTCAGGGCTCGAGTAGGTCACCCTGTACCTGGAAACTT
GCCCCTGTGGGCTTTCCCAAGCAATTTTGATGGAATCGACATCCACATCAGTGAATGCCAG
TCCTTTAGGGCGATCAATGTTGGTTACTGCAGTCTGAACCAGAGGCTGACTCTCCCGCTT
GGATTCTGAGCATAGACACTAACCACATACTCCACTGTGGGCTGCAAGCCTTCAATAGTCA
TTTCTGTTTGATCTGGACCTGCAGTTTTAAGTTTTTGTTGGNCCTGNNCCATTTTTGGGGAA
GGGGTGGTTACTCTTGTAACCAGTAACAGGGGAACTTGAAGCAGCCACTTGACACTAATG
CTGGTGGCCTGAACATCGGTCACTTGCATCTGGGATGGTTTGGTCAATTTCTGTTCGGTAAT
TAATGGGAAATTGGCTTACTGGCTTGCGGGGGGCTTCTCCACGGNCAGTGACAAGCATAC
ACAGGNGATGGGTATAATCAACTCCAGGTTTAAGGCCNCTGATGGTA

16510.2.edit

FIG. 15UU

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16511.1.edit

TCGAGCGGCCGCCGGGCAGGTCAGCGCTCTCAGGACGTCACCACCATGGCCTGGGCTCT
GCTCCTCACCCACCTCACTCAGGGCACAGGGTCTGGGCCCAGTCTGCCCTGACTCAG
CCTCCCTCCGCGTCCGGGTCTCCTGGACAGTCAGTCACCATCTCCTGCACTGGAACCAGCA
GTGACGTTGGTGCTTATGAATTTGTCTCCTGGTACCAACAACACCCCAGGCAAGGCCCCCAA
ACTCATGATTTCTGAGGTCACTAAGCGGCCCTCAGGGGTCCCTGATCGCTTCTCTGGCTCC
AAGTCTGGCAACACGGCCTCCCTGACCGTCTCTGGGCTCCANGCTGAGGATGANGCTGATT
ATTACTGGAAGCTCATATGCAGGCAACAACAATTGGGTGTTCGGCGGAAGGGACCAAGCT
GACCGTNCTAAGGTCAAGCCCAAGGCTTGCCCCCCTCGGTCACTCTTTCCCACCCTCCTCT
GAAGAAGCTTTCAAGCCCAACAANGNCACACTGGGTGTCTCCATAAGTGGACTTTCTACCC

16511.2.edit

16512.1.edit

AGCGTGGTCGCGGCCGAGGTCCAGCATCAGGAGCCCCGCCTTGCCGGCTCTGGTCATCGCC
TTTCTTTTGTGGCCTGAAACGATGTCATCACTTCGCAGTAGCAGAACTGCCGTCTCCACTG
CTGTCTTATAAGTCTGCAGCTTCACAGCCAATGGCTCCCATATGCCCAGTTCCTTCATGTCC
ACCAAAGTACCCGTCTCACCATTTACACCCCAGGTCTCACAGTTCTCCTGGGTGTGCTTGG
CCCGAAGGGAGGTAAGTANACGGATGGTGCTCGTCCCACAGTTCTCGGATCAGGGTACGAG
GAATGACCTCTAGGGCCTGGGCNACAAGCCCTGTCCCACAGTTCTGCCCGGGCCCGCTC
GA

16512.2.edit

TCGAGGGGCCGCCGGGCAGGTCCATACAGGGCTGTTGCCCAGGCCCTAGAGGNCATTCC
TTGTACCCTGATCCAGAACTGTGGGACCAGGCCATCCGTCTACTTACCTCCCTTCGGGCC
AAGCACACCCAGGAGAACTGTGAGACCTGGGGTGTAAATGGNGAGACGGGTACTTTGGTG
GACATGAAGGAACTGGGCATATGGGAGCCATTTGGCTGNGAAGCTGCANACTTATAAGACA
GCAGTGGAGACGGCAGTTCTGCTACTGCGAATTGATGACATCGTTTCAGGCCACAAAAAG
AAAGGCGATGACCANAGCCGGCAAGGCGGGGGCTTCCTGATGCTGGACCTCGGCCGCCGAC
CACGCTT

FIG. 15VV

AGCGTGGTCGCGGCCGAGGTCCACTAGAGGTCTGTGCCATTGCCCAGGCAGAGTCTCTG
CGTTACAAACTCCTAGGAGGGCTTGCTGTGCGGAGGGCCTGCTATGGTGTGCTGCGGTTCA
TCATGGAGAGTGGGGCCAAAGGCTGCGAGGTTGTGGTGTCTGGGAAACTCCGAGGACAGA
GGGCTAAATCCATGAAGTTTGTGGATGGCCTGATGATCCACAGCGGAGACCCTGTTAACTA
CTACGTTGACACTGCTGTGCGCCACGTGTTGCTCANACAGGGTGTGCTGGGCATCAAGGTG
AAGATCATGCTGCCCTGGGACCCANCTGGCAAAAATGGCCCTTAAAAACCCCTTGCCNTG
ACCACGTGAACCATTTGTGNGAACCCCAAGATGAANATACTTGCCCACCACCCCCCATTC

16514.2.edit

16515.1.edit

16515.2.edit

ANCGTGGTCGCGGCCGAGGTCCTCACCAGAGGTGNCACCTACAACATCATAGTGGAGGCACTGAAAGACGANCAGAGGCATAAGGTTCGGGAAGAGG

16516.2.edit

1651". Legir

ANCGNGGTCGCGGCCGANGTNTTTTTTCTTNTTTTTTT

16518.1.edir

AGCGTGGTCGCGGCCGAGGTCTGAGGTTACATGCGTGGTGGTGGACGTGAGCCACGAAGA
CCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAA
GCCGCGGGAGGAGCAGTACAACACACACGTACCGGGNGGTCAGCGTCCTCACCGTCCTGCA
CCAGAATTGGTTGAATGGCAAGGAGTACAAGNGCAAGGTTTCCAACAAAGCCNTCCCAGC
CCCNTCGAAAAAACCATTTCCAAAGCCAAAGGCAGCCCCGAGAACCACAGGTGTACAC
CCTGCCCCCATCCCGGGAGAAAAGANAACCNGGTTCAGCCTTAACTTGCTTGGTC
NAANGCTTTTTATCCCAACGNACTTCCCCCCNTGGAANTGGGAAAAACCAATGGGCCAANC

16513.2.adir

FIG. 15XX

AGCGTGGTCGCGGACGANGTCCTGTCAGAGTGGNACTGGTAGAAGTTCCANGAACCCTGA ACTGTAAGGGTTCTTCATCAGTGCCAACAGGATGACATGAAATGATGTACTCAGAAGNGN CCTGGAATGGGGCCCATGANATGGTTGCC

16519.2.edit

16520.1.edit

16520.2.edit

TCGAGCGGCCCCGGGCAGGTCCTTGCAGCTCTGCAGTGTCTTCTTCACCATCAGGTGCA GGGAATAGCTCATGGATTCCATCCTCAGGGCTCGAGTAGGTCACCCTGTACCTGGAAACTT GCCCCTGTGGGCTTTCCCCAAGCAATTTTGATGGAATCGACATCCACATCAGTGAATGCCAG TCCTTTAGGGCGATCAATGTTGGTTACTGCAGNCTGAACCAGAGGCTGACTCTCCCGCTT GGATTCTGAGCATAGACACTAACCACATACTCCACTGTGGGCTGCAANCCTTCAATAANNC

16521.2.edit

TCGAGCGGCCGGGGCAGGTCTGGTGGGGGTCCTGGCACACGCACATGGGGGNGTTGNT
CTNATCCAGCTGCCCAGCCCCCATTGGCGAGTTTGAGAAGGTGTGCAGCAATGACAACAA
NACCTTCGACTCTTCCTGCCACTTCTTTGCCACAAAGTGCACCCTGGAGGGCACCAAGAAG
GGCCACAAGCTCCACCTGGACTACATCGGGCCTTGCAAATACATCCCCCCTTGCCTGGACT
CTGAGCTGACCGAATTCCCCCTTGCGCATGCGGGACTGGCTCAAGAACCGTCCTGGCACCC
TTGTATGANAGGGATGAAGACACNACCC

FIG. 15YY

AGCGTGGTCGCGGCCGAGGTCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTG
GTGACCGTGGCCTCCAGCAACTTCGGCACCCAGACCTACACCTGCAACGTAGATCACAAGC
CCAGCAACACCAAGGTGGACAAGAGAGATTGAGCCCAAATCTTGTGACAAAACTCACACAT
GCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCGCAT
CCCCCTTCCAAACCTGCCCGGGCGGCGCTCGAAAGCCGAATTCCAGCACACTGGCGGCCG
GTACTAGTGGANCCNAACTTGGNANCCAACCTGGNGGAANTAATGGGCATAANCTGTTTC
TGGGGGGAAATTGGTATCCNGTTTACAATTCCCNCACAACATACGAGCCGGAAGCATAAA
AGNGTAAAAGCCTGGGGGNGGCCTANTGAAGTGAAGCTAAACTCACATTAATTNGCGTTG

16522.2.edit

TCGAGCGGCCGCCCGGGCAGGTTTGGAAGGGGGATGCGGGGGAAGAGAGACTGACGG TCCCCCAGGAGTTCAGGTGCTGGGCACGGTGGGCATGTGTGAGTTTTGTCACAAGATTTG GGCTCAACTCTCTTGTCCACCTTGGTGTTGCTGGGCTTGTGATCTACGTTGCAGGTGTAGGT CTGGGNGCCGAAGTTGCTGGAGGGCACGGTCACCACGCTGCTGAGGGAGTAGAGTCCTGA GGACTGTANGACAGACCTCGGCCGNGACCACGCTAAGCCGAATTCTGCAGATATCCATCA CACTGGCGGCCGCTCCGAGCATGCATTTTAGAGG

16523.1.edir

AGCGTGGNCGCGGACGANGACAACAACCCC

16523.2.edit

16524.1.edit

AGCGTGGTCGCGGCCGAGGTCCAGCCTGGAGATAANGGTGAAGGTGGTGCCCCCGGACTT
CCAGGTATAGCTGGACCTCGTGGTAGCCCTGGTGAGAGAGGTGAAACTGGCCCTCCAGGA
CCTGCTGGTTTCCCTGGTGCTCCTGGACAGAATGGTGAACCTGGNGGTAAAGGAGAGAAAGA
GGGGCTCCGGNTGANAAAGGTGAAGGAGGCCCTCCTGNATTGGCAGGGGCCCCANGACTT
AGAGGTGGAGCTGGCCCCCTGGCCCCGAAGGAGGAAAGG

FIG. 15ZZ

16524.2.edit

TCGAGCGCCGCCCGGGCAGGTCTGGGCCAGGAGGACCAATAGGACCAGTAGGACCCCTT GGGCCATCTTTCCCTGGGACACCATCAGCACCTGGACCGCCTGGTTCACCCTTGTCACCCTT TGGACCAGGACTTCCAAGACCTCCTCTTTCTCCAGGCATTCCTTGCAGACCAGGAGTACCA NCAGCACCAGGTGGCCCAGGAGGACCAGCAGCACCCTTTCCTCCTTCGGGACCAGGGGGA CCAGCTCCACCTCTAAGTCCTGGGGCCCCTGCCAATCCAGGAGGCCTCCTTCACCTTTCTC

16526.1.edit

TCGAGCGGCCGCCCGGGCAGGTCCACCGGGATATTCGGGGGGTCTGGCAGGAATGGGAGGCATCCAGAACGACGAGAAGGAGACCATGCAAAGCCTGAACGACCGCCTGGCCTCTTACCTGGACAGAGTGAGGAGCCTGGAGACCAAAATCCGGGAGCACATTACTTCAAGAAGAAGAGGAGCAAAATCCGAGGACCTGGAGGCCATTACTTCAAGATCATCGAGGACCTGAGGGCCCTCANATCTTCGCAAAATACTGCNGAGAATGCCCG

16526.2.edit

ATGCGNGGTCGCGGCCGANGACCANCTCTGGCTCATACTTGACTCTAAAGNCNTCACCAGNANTTACGGNCATTGCCAATCTGCAGAACCATGCGGGCATTGTCCGCANTATTTGCGAAGATCTGAGCCCTCAGGNCCTCGATGATCTTGAAGTAANGGCTCCAGTCTCTGACCTGGGGTCCTTCTTCTCCAAGTGCTCCCAGCCTCCGGTTCTCCAAGNCTTCTCCACTCCCAAGNCTTCTCCACTCTCCAAGNCTTCTCCACTCTCCAGGCCTCCGGTTCTCCAAGNCTTCTCCACTCTCCAGGCCTCCAGGCCTTTTGCATGGACT

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TCGAGCGGCCGCCGGGCAGGTCTGCCAACACCAAGATTGGCCCCCGCCGCATCCACACA GTTNGTGTGCGGGGAGGTAACAAGAAATACCGTGCCCTGAGGNTGGACGNGGGGAATTTC TCCTGGGGCTCAGAGTGTTGTACTCGTAAAACAAGGATCATCGATGTTGTCTACAATGCAT CTAATAACGAGCTGGTTCGTACCAAGACCCTGGTGAAGAATTGCATCGTGCTCATNGACA GCACACCGTACCGACAGTGGGTACCGAAGTCCCACTATGCNCCT

FIG. 15.4.4.4

TCGAGCGGCCGGGCAGGTCCACCACACCCAATTCCTTGCTGGTATCATGGCAGCCGC CACGTGCCAGGATTACCGGCTACATCATCAAGTATGAGAAGCCTGGGTCTCCTCCCAGAGA AGTGGTCCCTCGGCCCCTGGTGTCACAGAGGCTACTATTACTGGCCTGGAACCGGGA ACCGAATATACAATTTATGTCATTGCCCTGAAG

16528.2.edit

AGCGTGNTCNCGGCCGAGGATGGGGAAGCTCGNCTGTCTTTTTCCTTCCAATCAGGGGCTN
NNTCTTCTGATTATTCTTCAGGGCAANGACATAAATTGTATATTCGGNTCCCGGTTCCAGN
CCAGTAATAGTAGCCTCTGTGACACCAGGGCGGGGCCGAGGGACCACTTCTCTGGGAGGA
GACCCAGGCTTCTCATACTTGATGATGAAGCCGGTAATCCTGGCACGTGGGCGGCTGCCAT
GATACCACCAANGAATTGGGTGTGGTGGACCTGCCCGGGCGGCCGCTCGAAAANCCGAA
TTCNTGCAAGAATATCCATCACACTTGGGCGGGCCGNTCGAACCATGCATCNTAAAAGGG
CCCCAATTTCCCCCCCTATTAGGNGAAGCCNCATTTAACAAATTCCACTTGG

16529.1.edit

16529.2.edit

FIG. 15BBB

16530.2.edit

16531.1.edit

16531.2.edit

AGCGTGGTCGCGGCCGAGGTCTGTACTCGGAGCTAAGCAAACTGACCAATGACATTGAAG
AGCTGGGCCCCTACACCCTGGACAGGAACAGTCTCTATGTCAATGGTTTCACCCATCAGAG
CTCTGTGNCCACCACCAGCACTCCTGGGACCTCCACAGTGGATTTCAGAACCTCAGGGACT
CCATCCTCCCTCTCCAGCCCCACAATTATGGCTGCTGGCCCTCTCCTGGTACCATTCACCCT
CAACTTCACCATCACCAACCTGCAGTATGGGGAGGACATGGGTCACCCTGNCTCCAGGAA
GTTCAACACCACA

16532.1.edit -

FIG. 15CCC

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AGCGTGGTCGCGGGCGAGGTGAGCCACAGGTGACCGGGGCTGAAGCTGGGGCTGCTGGNC

02_16558.4.edit

CAGCNGCTCCNACGGGGCCTGNGGGACCAACAACACCGTTTTCACCCTTAGGCCCTTTGGC
TCCTCTTTCTCCTTTAGCACCAGGTTGACCAGCAGCNCCANCAGGACCAGCAAATCCATTG
GGGCCAGCAGGACCGACCTCACCACGTTCACCAGGGCTTCCCCGAGGACCAGCAGGACCA
GCAGGACCAGCAGCCCCAGCTTCGCCCCGGTCACCTGTGGCTCACCTCGGCCGCGACCACG
CT

03_16535.1.edit

04_16535.2.edit

AGCGNGGTCGCGGCCGAGGTCCAGCTCTGTCTCATACTTGACTCTAAAGTCATCAGCAGCA AGACGGGCATTGTCAATCTGCAGAACGATGCGGGGCATTGTCCGCAGTATTTGCGAAGATCT GAGCCCTCAGGTCCTCGATGATCTTGAAGTAATGGCTCCAGTCTCTGACCTGGGGTCCCTT CTTCTCCAAGTGCTCCCGGATTTTGCTCTCEAGCCTCCGGTTCTCGGTCTCCAGGCTCCTCA CTCTGTCCAGGTAAGAAGGCCCAGGCGGTCGTTCAGGCTTTGCATGGTCTCCTTCTCTTCT GGATGCCTCCCATTCCTGCCAGACCC

05_16536.1.edic

TCGAGCGGCCGGGCAGGTCAGGAAGCACATTGGTCTTAGAGCCACTGCCTCCTGGA TTCCACCTGTGCTGCGGACATCTCCAGGGAGTGCAGAAGGGAAGCAGGTCAAACTGCTCA GATCAGTCAGACTGGCTGTTCTCAGTTCTCACCTGAGCAAGGTCAGTCTGCAGCCAGAGTA CAGAGGGCCAACACTGGTGTTCTTGAACAAGGGCTTGAGCAGACCCTTGCAGAACCCTCTTC CGTGGTGTTGAACTTCCTGGAAACCAGGGTGTTGCATGTTTTTCCTCATAATGCAAGGTTG

FIG. 15DDD

07_16537.1.edit

08_16537_2.edit

TCGAGCGGTCGCCCGGGCAGGTTTCGTGACCGTGACCTCGAGGTGGACACCACCCTCAAG AGCCTGAGCCAGCAGATCGAGAACATCCGGAGCCCAGAGGGCAGCCGCAAGAACCCCGC CCGCACCTGCCGTGACCTCAAGATGTGCCACTCTGACTGGAAGAGTGGAGAGTACTGGAT TGACCCCAACCAAGGCTGCAACCTGGATGCCATCAAAGTCTTCTGCAACATGGAGACTGGT GAGACCTGCGTGTACCCCACTCAGCCCAGTGTGGGCCCAGAAGAAACTGGTACATCAGCA AGGAACCCCAAGGACAAGAGGCATTGTCTTGGTTCGGCGAGNAGCATGACCCGATGGATT CCAGTTTCGAGTATTGGCGGCCAGGGCTTCCCGACCCTTGCCGATGGACCTCGGCCGCG

FIG. 15EEE

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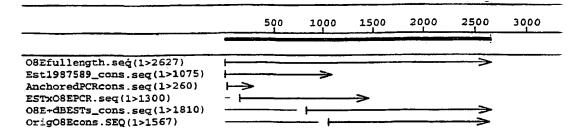
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- (71) Applicant: CORIXA CORPORATION [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US).

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF OVARIAN CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as ovarian cancer, are disclosed. Compositions may comprise one or more ovarian carcinoma proteins, immunogenic portions thereof, polynucleotides that encode such portions or antibodies or immune system cells specific for such proteins. Such compositions may be used, for example, for the prevention and treatment of diseases such as ovarian cancer. Methods are further provided for identifying tumor antigens that are secreted from ovarian carcinomas and/or other tumors. Polypeptides and polynucleotides as provided herein may further be used for the diagnosis and monitoring of ovarian cancer.



O 00/36107 A3

INTERNATIONAL SEARCH REPORT

Inter onal Application No PCT/US 99/30270

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ÎPC 7	FICATION OF SUBJECT MATTER C12N15/12 C07K14/47 C12N15 G01N33/68 C07K16/18	/62 C12N15/11	C12Q1/68	
According t	o International Patent Classification (IPC) or to both national classifi	cation and IPC		
	SEARCHED	cation and IPC		
Minimum de	ocumentation searched (classification system followed by classifica	tion symbols)		
IPC 7	C12N C07K C12Q G01N			
Documenta	tion searched other than minimum documentation to the extent that	such documents are included in the	fields searched	
Electronic d	ata base consulted during the international search (name of data b	ase and where practical search ton	ms used)	
C. DOCUM	ENTS CONSIDERED TO BE RELEVANT			
Category °	Citation of document, with indication, where appropriate, of the re	elevant passages	Relevant to claim No.	
X	K. ISHIKAWA ET AL.: "Prediction coding sequences of unidentified	of the	3,4,6	
	genes. The complete sequences of	100 new		
	cDNA clones from brain which car	code for		
	large proteins in vitro." DNA RES.,			
	vol. 5, 1998, pages 169-176, XPG	002121149		
	the whole document			
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<u> </u>	ner documents are listed in the continuation of box C.	Patent family members an	e listed in annex.	
	egories of cited documents :	T later document published after	the international filing date	
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other n	neans	document is combined with on ments, such combination being	e or more other such docu-	
	nt published prior to the international filing date but an the priority date claimed	in the art. "&" document member of the same	patent family	
Date of the a	ctual completion of the international search	Date of mailing of the internation	•	
15	15 May 2000		B. 2000 .	
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	European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk			
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INTERNATIONAL SEARCH REPORT

Interr nal Application No
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C.(Continua Category °	ation) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.
Category	Chauth of document, with indication, where appropriate, or the relevant passages		Relevant to claim No.
Α	MA J ET AL: "USE OF ENCAPSULATED SINGLE CHAIN ANTIBODIES FOR INDUCTION OF ANTI-IDIOTYPIC HUMORAL AND CELLULAR IMMUNE RESPONSES" JOURNAL OF PHARMACEUTICAL SCIENCES,US,AMERICAN PHARMACEUTICAL ASSOCIATION. WASHINGTON, vol. 87, no. 11, November 1998 (1998-11), pages 1375-1378, XP000877492 ISSN: 0022-3549 the whole document		
Α	GILLESPIE A M ET AL: "MAGE, BAGE AND GAGE: TUMOUR ANTIGEN EXPRESSION IN BENIGN AND MALIGNANT OVARIAN TISSUE" BRITISH JOURNAL OF CANCER, GB, LONDON, vol. 78, no. 6, September 1998 (1998-09), pages 816-821, XP000892404 ISSN: 0007-0920 the whole document		
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			-

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

1

Intelliational application No. PCT/US 99/30270

INTERNATIONAL SEARCH REPORT

Box !	Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
	Although claims 18 to 20, 27, 28, 35 to 41, 46 to 48 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Int	ernational Searching Authority found multiple inventions in this international application, as follows:
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
·	
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. 🗶	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
	1-68 (partially)
Remai	rk on Protest The additional search fees were accompanied by the applicant's protest.
	No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1998)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-68 {partially}

An isolated polypeptide comprising at least an immunogenic portion of an ovarian carcinoma protein and encoded by SEQ ID NO:1, expression vectors comprising said polynucleotide, host cells transformed by said vector, pharmaceutical compositions and vaccines comprising the polypeptide encoded by said polynuceotide according to claims 9 to 17, 23 to 25 and 29 to 34, and methods of using said polynucleotides for the treatment and/or diagnosis of ovarian cancer and diagnostic kits comprising said polynucleotide.

BNSDOCID: <WO____0036107A3_I_>

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